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ABSTRACT

The text of three separate Congressional hearings on medical devices and drug issues is presented in this document. The first hearing considers the need for legislation to control potential abuses and illegal diversion of human growth hormone which is produced by using recombinant deoxyribonucleic acid (DNA) technology. The second hearing investigates the dramatic and continuing price increases for prescription drugs, particularly whether the reasons cited by the drug industry for these increases have any basis in fact. The third hearing is on the Federal Drug Association's implementation of the Medical Devices Amendments of 1976. Testimony from 33 witnesses, including government regulators, representatives from advocacy groups, victims and their relatives, representatives from industry, and medical experts is presented. Materials submitted for the record are included. (ABL)

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MEDICAL DEVICES AND DRUG ISSUES

HEARINGS

BEFORE THE

SUBCOMMITTEE ON
HEALTH AND THE ENVIRONMENT

OF THE

COMMITTEE ON
ENERGY AND COMMERCE
HOUSE OF REPRESENTATIVES

ONE HUNDREDTH CONGRESS

FIRST SESSION

APRIL 8, 21, AND MAY 4, 1987

Serial No. 100-34

Printed for the use of the Committee on Energy and Commerce

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MEDICAL DEVICES AND DRUG ISSUES
Illicit Diversion and Abuse of Human Growth Hormone

WEDNESDAY, APRIL 8, 1987

House of Representatives,
Committee on Energy and Commerce,
Subcommittee on Health and the Environment,
Washington, DC.

The subcommittee met, pursuant to notice, at 9:15 a.m., in room 2218, Rayburn House Office Building, Hon. Henry A. Waxman (chairman) presiding.

Mr. **Waxman**. The meeting of the subcommittee will come to order. Today we will be considering the need for legislation to control potential abuses and illegal diversion of human growth hormone. Human growth hormone, produced by using recombinant DNA technology, truly represents a modern scientific miracle. Children whose bodies do not produce sufficient growth hormone are known as pituitary dwarfes. In the past growth hormone from cadavers greatly improved the growth-deficient child's prospects of attaining a more nearly normal adult height. Unfortunately, the supply was always limited, and in 1985 these children faced a catastrophe when that natural source of the hormone was withdrawn after being found to be contaminated with a deadly slow virus.

In 1985, the Food & Drug Administration quickly approved a genetically engineered human growth hormone which has restored hope to the families of these children. The use of genetic engineering assured these families that the history of shortages would end forever.

Unfortunately, as we will hear today, it appears that the potentially limitless supply of human growth hormone has brought with it the possibility of serious abuse. A growing number of physicians and public health specialists are concerned about the reported use of growth hormone by athletes. There is a genuine risk that growth hormones will be soon used to treat obesity, to make tall children taller, to make normal children tall, and to slow the aging process, all without scientific evidence that the drug would be either safe or effective for such uses.

Safety and effectiveness are the basic concerns of all of our laws regulating drugs. Once the FDA has approved a drug as safe and effective for a particular indication, medical practice generally determines whether the drug is used for other purposes.

At this time artificially produced human growth hormone has been approved by the FDA for one and only one use. That use is the long term treatment of children who have growth failure due to a lack of adequate growth hormone secretion by their own bodies.

However, as we will hear this morning, human growth hormone presents unique pressures for diversion to other potentially dangerous uses.

Today physicians are being pressed to prescribe the drug for normal healthy children, who are simply somewhat short for their age. They are also being pressured by parents to boost the height of children who are actually tall, in the hope of making them even taller.

Equally ominous is the apparent development of a black market in human growth hormone outside of the control of physicians. It would be a terrible mistake to allow this drug to be abused in this way.

Nothing we do should in any way hinder the appropriate use of human growth hormone, nor should we impede scientific research on the appropriateness of other uses. Children who meet the current indications should have full access to this wonderful substance.

A number of physicians, including the Chief Medical Officer for the U.S. Olympic Committee, who will be with us this morning, have suggested placing this hormone in Schedule II of the Controlled Substances Act. Classification of artificial human growth hormone as a controlled substance would in no way limit the proper use of this drug, nor would it inhibit necessary research.

Some of today's witnesses have raised questions about this approach, and we certainly intend to listen to their concerns carefully; but we must also listen seriously and respond to the concerns of those who see this product being diverted to inappropriate and even potentially dangerous uses.

I regret that due to the Full Committee mark-up scheduled this morning, the subcommittee will adjourn this morning at approximately 10:30 a.m. We will reconvene later this afternoon in room 2123 of this building, at 2 o'clock, or following completion of the Full Committee agenda, so we will have to leave that on some kind of tentative basis as to when we will reconvene again.

Our first witnesses this morning have been asked to help us understand whether the current voluntary system of distributing human growth hormone is adequate to prevent diversion and illicit use.

Tam Thompson is an athlete from the University of Texas. Prof. Terry Todd is an expert in the study of mechanics and anatomy in relation to human movement and athletic performance at the University of Texas. He is a former power lifter. Robert Voy is a physician who serves as a Director of Sports Medicine and Chief Medical Officer of the U.S. Olympics Committee. William Taylor is a physician with the Student Health Service at Washington State University. He has written widely on the subject of the use of drugs by athletes, including a recent book, "Hormonal Manipulation: A New Era of Monstrous Athletes." Robert Kerr is a physician from San Gabriel, CA. Thomas Sodeman is a physician with the Department of Pathology at Texas Tech University. Dr. Sodeman is appearing on behalf of the College of American Pathologists.

I would like to ask each of these individuals to come forward and take seats at our table.

We want to welcome you to our subcommittee hearing this morning. We appreciate your being here. We have prepared statements from you, and those prepared statements will be put in the record in full and complete.

What we would like to ask each of you to do is to summarize for us the highlights of your views in no more than 5 minutes. Please keep pretty close to the 5-minute time, so that we can complete the whole agenda and hear from the witnesses and have an opportunity for questions and answers.

We have a timer. When the bell rings, that will be an indication that the 5 minutes is up, so that we can keep track of the schedule for the hearing today.

I want to ask Tam Thompson to start first, if you would. We appreciate your being here. I think it took a lot of courage for you to come today to talk about your personal drive and the temptation all athletes face, and what you see as the potential problems that we ought to deal with, this drug.

STATEMENTS OF TAM THOMPSON, UNIVERSITY OF TEXAS; THOMAS SODEMAN, ON BEHALF OF COLLEGE OF AMERICAN PATHOLOGISTS; TERRY TODD, PROFESSOR OF KINESIOLOGY, UNIVERSITY OF TEXAS; ROBERT VOY, UNITED STATES OLYMPIC COMMITTEE; WILLIAM N. TAYLOR, STUDENT HEALTH CENTER, WASHINGTON STATE UNIVERSITY AND ALSO ON BEHALF OF AMERICAN COLLEGE OF SPORTS MEDICINE; AND ROBERT B. KERR, SAN GABRIEL, CA

Ms. THOMPSON. Well, I'm 28 years old. I'm a graduate student at the University of Texas, and a teaching assistant, first year master's in biomechanics. I have a Bachelor of Science Degree in Physical Education.

I have been lifting and running for about 9 years, and I started out as a long distance runner for the University of Houston. There was talk then, about 6 years ago, of steroids, and nobody really knew what they were, and they didn't know anything about growth hormone. I have been competing in power lifting 4½ years. I went to my first meet, not having taken any drugs, got sixth place out of nine, and kind of succumbed to the notion that the other women beat me because they were taking drugs. People I trained with reinforced that, so I figured I'd get on them, too. And after taking steroids on and off for 1½ years, I figured that growth hormones sounded like a good deal, because supposedly the muscle gains that athletes make on growth hormone are permanent. They don't wear off like they do with steroids. Any muscle tissue, supposedly, that you gain and supposedly there are these tremendous gains of 30 or 40 pounds of muscle in 2 months or something like that, I was promised that this would be permanent. I was also told that there would be increased tendon and ligament strength.

I was also told that if you are under the age of 23 or 25, you would gain an inch of height on this stuff, and I was about 23, 24 at the time, and that was very attractive to me, being 5 feet 2 inches.

So I went on the growth hormone. It was very easy to obtain. The people I trained with at the gym made it known to me that it was available if I wanted it. The only problems that I ever had in obtaining it was that the man supplying it would run out of it, it went that quickly. There was a guy in Pasadena, TX selling it, and this was before the synthetic came out, this was the summer of 1984, when it was the authentic growth hormone from cadavers. Since then I understand—I keep in touch with him—that he has the Somatatrophin and he can get a much larger supply.

The only thing that held me back from taking a whole lot of it was the price. It was approximately $80 a week cost for a 7-week cycle of it, about $560. I have seen other athletes go into debt to buy this stuff, because the people that sell it are very lenient about giving credit, they will mail it to you. They have mailing lists that they will send out to you through the mail and you can mail-order it, and you can have it Federal Expressed.

I had a young friend of mine who was 16 years old that played basketball for Deer Park. She was already 6 feet tall, but she wanted me to get her some, because she wanted to be a better basketball player, and I have had a friend of mine had a male friend in Houston send her some steroids up to Dallas, unsolicited, and he just sent her a box of them and said here, why don't you take these. They'll make you a better power lifter. And she had enough sense to send them back, but sometimes you have those cases where even if the athlete isn't even soliciting drugs or isn't even looking for growth hormone or steroids, people will offer it to you if you're any good. You'll have these little sponsors that tend to spring up, and they want to help you out, or sometimes they work like the narcotics pushers, I guess. They give you a little for free, and they get you hooked on the gains you're making.

In the case of steroids, it's not addicting. You don't get addicted to it, but there is this ego thing that you see your strength rising, and you get bigger, and people tend to like that a lot, so they keep on using it.

I used one cycle of it myself for 7 weeks, and I was told to eat as many calories as I could, because that would make a muscle gain. I was also told that it would run the fat percent down, and to a lot of women I have talked to, that's very attractive, running fat percent down.

The thing also—there might have been a little twinge of conscience holding back some of the athletes, because the growth hormone that was the real thing from cadavers was in short supply, and we realized that a lot of children needed that, and that kind of tugged at me, but then after the synthetic came out, now there's nothing to hold them back, and there's no drug test that I know of for growth hormone, and athletes know this, that they can take it right up to a national or world competition and it won't be detected, and they'll slide right through, unlike steroids. So there's really nothing to hold them back, other than cost now, and there are always those sponsors who are willing to buy you things.

I have people who pay my airfare to national meets, and to go from paying airfare and hotel to buying you drugs is not that big a step.

There have also been some cases I know of, of bad stuff being sold like one of my friends sold $1,500 worth of distilled water to another one, and told him it was growth hormone. The guy found out because he had it tested by the lab at Texas A&M. There's been those two instances of people dying from a bad lot.

So the main problem I had with it was mainly the problem of comparison shopping, to find out where I could get the best price. I had a guy that would sell it to me for $80 a package in Pasadena, and then this one that offered to mail it to me from Bryan College Station for $70. So I bought it from him. It was mainly a matter of shopping around to find the right price.

That's about all I have to say.

Mr. **Waxman**. Thank you very much.

Dr. Sodeman, we will hear from you next. Would you pull the microphone over.

STATEMENT OF THOMAS SODEMAN

Mr. **Sodeman**. Mr. Chairman and Mr. Coats, my name is Thomas Sodeman. I am a board-certified pathologist and professor and chairman of the Department of Pathology and associate dean for clinical affairs at Texas Tech University Medical School.

I am appearing here today on behalf of the College of American Pathologists, a national medical specialty society, representing more than 10,000 pathologists who practice medicine in community hospitals, teaching hospitals, and reference laboratories.

The College of American Pathologists is pleased to present to the Health and Environmental Subcommittee its concerns for reasonable control of the new synthetically produced growth hormone. We support the proposed legislation to place growth hormone under Schedule 2 of the Controlled Substance Act.

The College of American Pathologists has a long history of involvement with issues of pituitary growth hormone and the needs of children deficient in this important substance.

Having first become involved in the collection of pituitaries at autopsies in the 1960s, the College in 1963 was instrumental in establishing the national pituitary agency aided by a grant from the National Institutes of Health. The College has continued that early interest in growth hormone, encouraging pathologists to harvest pituitaries at autopsies by setting on the board of the National Pituitary Program, and prior to the halt of the distribution of hormones, organizing a grass roots effort within the State legislatures that would facilitate the removal of pituitaries at autopsy.

The need to continue to collect pituitaries at autopsies for further study in hormones still remains present.

On the issue at hand today, the College's foremost concern is that growth hormone continues to be available for the approximately 10,000 patients for whom it is medically necessary.

The newly produced synthetic growth hormone will afford a greater opportunity to treat hormone deficiencies with less risk to the patient. Potential usefulness in treatment and other applications such as burn patients, for wound healing, osteoporosis, delayed puberty, aging, are now under study, and only continued controlled use will provide the necessary scientific information to assure appropriate medical application, and to assure short and long term adverse effects.

Unlimited and controlled distribution could lead to abuse of this very powerful substance. The potential pressures that will be brought on practitioners with the release of this hormone by parents who have short children will be tremendous.

These parents may see a potential to adjust the normal, natural process of individual difference to fit their desire for a tall child.

We cannot allow the social pressures to prematurely release in an uncontrolled manner this drug when there is insufficient scientific data to know what the long term consequences of use will be. Questions are not answered as to how this product will act on the normal population. A widely publicized statement that this is risk-free is misleading. The risk of transmission of infection is eliminated, but the risk to patients' natural well being is yet to be assessed.

The College is concerned about the development of a black market availability of these drugs. While the social pressures of some parents may be strong, there is even a greater pressure among the junior and senior high school children.

We already see among this group the abuse of the anabolic steroids in an effort to develop muscle mass and size. The ability to substantially change one's physical appearance in what is perceived as a positive manner in as little as 8 to 16 weeks has brought anabolic steroids into the black market and into the hands of children.

Efforts to explain the long-term effects of increased cardiac disease and sterility have gone unheeded. The availability of growth hormone, which would have a more lasting effect and potentially a more dramatic effect, will certainly lead to abuse.

The drug program that I run at Lubbock, TX on both junior high and high school students an on athletes at Texas Tech University greatly concern me, because of our inability to test for this particular agent.

Of equal concern for abuse is the use of growth hormones by athletes. A massive national program is developing to control steroid abuse and similar drugs by competitive athletes because of the unfair advantage that these drugs provide. The tremendous peer pressure to win, and the potential economic pressures to win have resulted in a national problem.

Growth hormone is among those drugs that are banned, and the potential damage to the young athlete by abuse of growth hormone is unknown.

Inclusion in Schedule 2 is essential to control the access of growth hormone into the athletic drug black market.

While the college members have addressed methods to monitor the presence of drugs of abuse, steroids and growth hormones present difficult testing problems. Testing of anabolic steroids is limited to less than a half dozen laboratories in this country. Insufficient research is available for some of these steroids and anabolic hormones to distinguish between natural levels and levels obtained in abuse cases. The cost of developing more and better testing procedures and to equip laboratories for such testing is astronomical.

While testing is readily available for growth hormone, there is insufficient data for normal variation of growth hormone to assure detection of abuse, and the half-life is too short for adequate monitoring.

In summary, the College of American Pathologists supports the development of controls on growth hormone to prevent inappropriate, insufficiently tested applications. We agree that such a move reflects a responsible attitude, while medical scientists continue to unravel the key to its potential use.

Abuse of this hormone is potentially great, and every attempt should be made to avoid a similar inappropriate and dangerous use of this hormone as has developed with anabolic steroids.

Thank you, Mr. Chairman.

[Mr. Sodeman's prepared statement follows:]

STATEMENT OF THE COLLEGE OF AMERICAN PATHOLOGISTS

Mr. Chairman and members of the subcommittee, my name is Thomas Sodeman, MD. I am a board-certified pathologist and professor and chairman of the Department of Pathology and Assistant Dean for Clinical Affairs at the Texas Tech University Medical School Health Sciences Center. I am appearing today on behalf of the College of American Pathologists, a national medical specialty society representing more than 10,000 pathologists who practice medicine in community and teaching hospitals and in independent laboratories.

The College of American Pathologists, is pleased to present to the Health and Environment Subcommittee its concerns for reasonable control of the new synthetically produced growth hormone. We support the proposed legislation to place growth hormone under Schedule II of the Controlled Substance Act.

The College of American Pathologists has a long history of involvement with the issue of pituitary growth hormone and the needs of children deficient in this important substance. The College first became involved in collecting pituitaries at autopsy for growth hormone in the early sixties when the parent of a growth-deficient child asked the College for help in collecting glands. At the time, there were pathologists collecting pituitaries for groups of other physicians, and it became obvious that these scattered collection programs needed to be focused and organized nationally. The College, in 1963, was instrumental in establishing the National Pituitary Agency—now the National Hormone and Pituitary Program—aided by a grant from the National Institutes of Health.

The College has continued that early interest in growth hormone collection; encouraging pathologists to collect pituitaries; sitting on the Board of the National Hormone and Pituitary Program; and, prior to the halt of distribution of the natural hormone, organizing a grassroots effort on the State level to enact legislation that would facilitate the removal of pituitaries at autopsy.

In March of 1985, the Federal Government took the precaution of halting the distribution of pituitary growth hormone after a rare disease, Creutzfeld-Jacob Disease, was associated with three deaths in recipients of the hormone. In the fall of 1985, the FDA approved the genetically engineered growth hormone and, in doing so, assured that growth-deficient children would finally have an adequate supply and a chance to develop normal growth.

While the synthetic growth hormone is indeed a blessing for those children, we at the College believe that the care that has been given to this issue must continue because of the potential for abuse and insufficiently tested applications of growth hormone. In addition, there still remains a need to collect pituitaries at autopsy since the research needs are not limited to growth hormone. Considerable endocrinologic research is underway: only 20 percent of the glycoproteins in the pituitary have been identified, leaving another 80 percent of unexplored territory.

On the issue at hand today, the control of untested and potentially dangerous applications of synthetic growth hormone for such various uses as dieting, athletic training, and a myriad of other applications, we believe that the scientific evidence is not yet available to safely suggest such experimentation prior to controlled studies.

The College's foremost concern is that growth hormone continues to be available to those approximately 10,000 patients for whom it is medically necessary. The newly produced synthetic growth hormone will afford a greater opportunity to treat hormone deficiencies with less risk to patients.

The potential usefulness in treatment of other applications such as burn patients to help wound healing, osteoporosis, delayed puberty, and aging are under study. Only continued controlled use will provide the necessary scientific information to assure appropriate medical applications and to assess short or long term adverse effects.

PARENTAL PRESSURES ON MEDICAL PRACTITIONERS

Unlimited and uncontrolled distribution could lead to abuse of this powerful substance. The potential pressures that will be brought to bear on the medical practitioner with release of a readily available supply of growth hormone will be tremendous. Parents who have short children may see a potential to adjust the normal natural process of individual difference to fit their specific desire for a tall child. In addition, the medical profession clearly recognizes a group of children who produce insufficient quantities of growth hormone but are *not* growth hormone deficient. This area is a medical "gray zone" that still requires medical judgment. There is no set rule that easily distinguishes these borderline children from those who naturally produce lower amounts of hormone and are shorter. In the past, there was insufficient naturally produced growth hormone to provide to these children. Social pressures are likely to bring some of these parents to potential sources of the hormone.

We can not allow social pressures to prematurely release in an uncontrolled manner this drug when there is insufficient scientific data to know the long term consequences of use in a borderline population. Questions are not answered as to how the products will act in a normal population. The widely publicized statement that these are "free of risk" is misleading. The risk of transmission of infection is eliminated; the risk to patients natural well being is yet to be determined.

The College is concerned about the development of a black market availability of these drugs. While the social pressures on some parents may be strong, there is even greater peer pressure among junior and senior high school children. We already see among this group the abuse of anabolic steroids in a effort to develop muscle mass and size. The ability to substantially change one's physical appearance, in what is perceived as a positive manner, in as little as 8 to 16 weeks has brought anabolic steroids to the black market and into the hands of children. Efforts to explain the long term effects of increased cardiac disease and sterility have gone unheeded. The availability of growth hormone which would have a more lasting effect and potentially a more dramatic effect will make the potential for abuse even greater.

ABUSE BY ATHLETES

Of equal concern for abuse is the use of growth hormone by athletes. A massive national program is developing to control abuse of steroids and similar drugs by competitive athletes. The unfair advantage provided by those drugs is stimulated by the tremendous peer group pressure to win and the potential economic gains of winning. This is a national problem. Growth hormone is among the drugs that are banned. The potential damage to young athletes by abuse of growth hormone is unknown. The advantage to the athlete in terms of increased muscle mass and muscle fiber size, the anabolic effect on protein and stimulation of fat tilization in preference to protein, all are productive to athletic performance. Inclusion in Schedule II is essential to controlling access of growth hormone into the athletic drug black market.

OTHER APPLICATIONS

Another potential use of growth hormone is for weight control. Growth hormone may provide a basis to preserve protein (muscle mass) during weight loss. It is known in this area, and abuse of growth hormone as part of a diet program could be significant.

LACK OF MONITORING

The use of this hormone by physicians in patients with medical indications is closely monitored: patients are checked for bone growth on a regular basis. Because of the diabetogenic actions, patients are followed for hyperglycemia and ketosis. As a replacement for those patients who do not have growth hormone, complications are uncommon.

The potential for serious harm in an uncontrolled abuse situation is great. For those who wish to supplement normal levels, we are less certain as to the side effects or the length of time before complications may be manifest. Our knowledge is limited mostly to patients who have growth hormone secreting tumors. Excessive bone growth and bone distortion, sweating, joint problems, muscle pains, cardiovascular and diabetic problems have all been reported.

TESTING PROBLEMS

While the College members have addressed methods to monitor the presence of drugs of abuse, steroids and growth hormone present difficult testing problems. Testing of anabolic steroids is limited to a half dozen laboratories in this country. Insufficient research is available for some of these steroids to distinguish between natural levels and levels obtained in abuse cases. The cost of developing more and better testing procedures and to equip laboratories for such testing is astronomical. While testing is readily available for growth hormone, there is insufficient data of the normal variation of growth hormone to assure detection of abuse. The production of growth hormone identical to natural hormone will not permit separation in the testing process. Ideally, an inert marker on the synthetic product could permit testing that would distinguish abuse from natural production. In the absence of such a market, laboratories will be severely limited in their abilities to detect abusers.

SUMMARY

The College of American Pathologists supports the development of controls on growth hormone to prevent inappropriate and insufficiently tested applications. We agree that such a move reflects a responsible attitude while medical scientists continue to unravel the keys to its potential use. Abuse of this hormone is potentially great, and every attempt should be made to avoid a similar inappropriate and dangerous use of this hormone as has developed with anabolic steroids.

Mr. WAXMAN. Thank you very much, Dr. Sodeman.

Dr. Todd, we will hear from you next.

STATEMENT OF TERRY TODD

Mr. TODD. Mr. Chairman and Mr. Coats, I am here to speak in support of the control of this substance. I began to take anabolic steroids myself 25 years ago. At that time, they were new, and they were used only by elite athletes, just a handful of elite athletes. Now they are used by hundreds of thousands of people, millions probably, most of whom are neither elite athletes or athletes at all, unless you consider recreational weight training athletics.

A recent report, for instance, revealed that in one high school in Florida, 65 percent of the male students were using anabolic steroids in hopes of turning themselves into some facsimile of Rambo or Schwartzenegger or some such superhero.

Steroids are, to be sure, still used by athletes, and their use is so widespread in certain sports, especially at the top levels, that it poses a major threat to health, as well as to fair play.

It has been over 20 years since I used steroids, but during that 20 years I have watched their use very closely, and this use has increased so dramatically that I have begun to speak out against them, and I do believe that had these drugs been classified as controlled substances 25 years ago, just after they were developed, it is a virtual certainty that some of the physiological and psychological that these drugs have caused would never have happened.

The story of steroids is a very sad story, but perhaps it can serve us as a cautionary tale where growth hormone is concerned. In the 1960's, hearings very much like this 1 were held about steroids, but nothing was done. Nothing was done.

I think that in the case of HGH, it is critical that we move as quickly as possible to impose some sort of control, because it seems clear that there are many more potential problems with HGH than we have seen already develop with steroids, and I don't say that likely.

And in case if anyone wonders if athletes will take HGH once the market economics brings the price of synthetic HGH down and once they are much more available, I think all you have to do is realize that two studies have been done, one on a group of runners, one on a group of lifters, and in both cases these people were asked if they would take a certain substance, unnamed, that would make them a national or world or olympic champion but would also kill them within 1 year, over 50 percent of the athletes in each group—in each group, and these were not absolute world class people—over 50 percent said they would be willing to die in order to achieve that athletic prominence.

No growth hormone itself is much, much more recent in origin as far as its use by athletes is concerned. The early to the mid-1970's is really when it began, and it's real use only began to explode in the early 1980's. The most dramatic example, I suppose, that I came across in the many, many interviews I've done about this is that one man told me that in his area of the country, which is a relatively isolated area, not very much population, there were 60 people in that area that were taking the growth hormone, and they were just football players, 60 football players, either college, NFL, or USFL—60 people were using the human growth hormone.

There is no question in my mind that if HGH does prove, as we know more and more about it, to be strongly anabolic, to be a strong muscle-building drug or substance, then their use will increase in the future, and it will increase enormously. It's a very short hop from H.G. Wells to HGH.

But what about the potential impact on HGH on fields other than sports, which perhaps is even more important? What about all the people in the world who would just like their children to be a few inches taller? What about this sort of cosmetic endocrinology?

Study after study has shown that height is an advantage both socially and economically. One study said each inch was worth $400. Another study found that when people chose between equally qualified candidates for a job, one tall, one short, the taller candidate was preferred by 72 percent of the people, the shorter candidate by only 1 percent. The other 27 percent had no preference.

Even our language reflects this sort of preference. We speak of, "It's mighty big of you." People are "small minded." We "look up" to people and so on.

The hard question is this: Should we make this drug only available to those like growth hormone deficient children, who need it really to overcome a disability, or should we also make it available to those who want it, so they can overcome their perceived relative disadvantage?

We need to decide, for instance, is giving GH to a child to make him 6 feet 2 inches instead of 5 feet 9 inches any different than fitting him with braces? A researcher in England says that he thinks very soon it will be as common as orthodontia.

But are we really prepared for a society in which the height difference between rich and poor will be dramatically evident—rich and poor people, rich and poor classes in any country, and the difference between rich and poor countries altogether.

But leaving aside the height question for just a moment, what about the use of HGH as a reducing aid? Studies suggest that it is only a matter of time before procedures are worked out that will enable a person to become and remain relatively lean and fat-free by taking growth hormone. Can anyone even imagine the implications of this? The question has to be asked: Would people with access to such a wonder drug even bother to exercise? And if the answer is no, what effect would this have on our Nation's cardiovascular health and on health care costs.

These questions are so complex and important that we should be very careful as we decided whether this powerful substance should continue to be available to any doctor who is now willing to prescribe it, as is now the case.

This is the first synthetic hormone to tempt us to improve on human nature. We have moved past life in the fast lane, and now we're in the Faust lane, and we need to be aware of the Mephistophelian consequences of our decision or our indecision. We need to be aware that if the story of steroids and HGH in athletics tells us anything, it tells that people are not only willing, they are anxious to swallow or inject substances that will change their appearance. We need to be aware that we may soon, to our sorrow, learn the answer to that question posed years ago by William Butler Yeats: "And what rough beast, it's hour come round at last, slouches toward Bethlehem to be born?"

Mr. WAXMAN. Thank you very much, Mr. Todd.

Dr. Voy?

STATEMENT OF ROBERT VOY

Mr. VOY. Mr. Chairman, my name is Robert Voy. I am chief medical officer and director of sports medicine and science at the U.S. Olympic Committee, and my offices are located at the U.S. Olympic Training Center in Colorado Springs.

I am here to present the current United States Olympic Committee policies regarding the abuse of growth hormone, whether it is human, animal, or synthetic.

For the past year, the U.S. Olympic Committee has been aware of the increasing abuse of this substance, particularly by athletes in power sports such as weightlifting, heavyweight wrestling, judo, and the field and track events.

These policies were expressed to the Scientific Affairs Committee of the AMA at its 1986 annual meeting, with the recommendation to place growth hormone under the Federal Controlled Substance Act as a Class 2 controlled substance. Thus far, the AMA has not ruled on this request.

In the last few months, the USOC Substance Abuse Research and Education Committee, through its athlete contacts and reports from its National Drug Control Hotline, has become increasingly concerned about the improper use of this substance by athletes. In fact, the committee will meet this weekend in Houston, TX to further discuss and consider solutions to this very complex problem.

Unlike other drugs considered to enhance athletic performance, the use of which is controlled by drug testing, which we've had a great deal of experience in, no urinalysis test at present exists for the detection of human or synthetic growth hormone. Nonetheless and notwithstanding the lack thereof, the U.S. Olympic Committee is convinced that this substance will become increasingly abused in sport. The U.S. Olympic Committee therefore established policy which states:

"That the use of growth hormone is prohibited, and any evidence confirming use will be cause for punitive action, comparable to that for using a banned substance—that is, immediate loss of eligibility by the national governing body for the sport and suspension from the U.S. Olympic Committee-sponsored activities for a minimum of 6 months from the date of specimen collection. Further, if found positive a second time, the athlete will be disqualified by the national governing body action for not less than 4 years."

It is important to note that the United States Olympic Committee policy states in addition that any person, whether that be physician, coach, trainer or whomever, shown to have aided or abetted the offense causing an athlete's qualification shall be suspended from all national governing body and U.S. Olympic Committee programs for not less than the period of the athlete's disqualification.

Now the adverse effects, health effects of growth hormone use are many and have been well documented. Not only does growth hormone cause muscle growth, but it also causes other body tissues to grow likewise. For example, there is an increase in skin thickness, increase in internal organ size, bones and facial features. It also increases laxity of muscles and decreases the protective fat surrounding the abdominal organs, making this a difficult situation and a risk in athletes in contact sports.

When present in excess of normal levels, it causes the disease, acromegaly, which consists of changes in the head and skull, enlargement of the fingers, ears, nose and toes, diabetes, heart disease, thyroid disease, menstrual disorders, decrease in sexual desire, impotence, and shortened lifespan—all well documented.

To my knowledge, no statistical evidence exists as to the incidence of growth hormone use amongst athletes. The United States Olympic Committee does, however, log firsthand information from athletes through its National Drug Control Hotline. I can therefore safely state, based on documented phone conversations, that since the marketing of synthetic growth hormone, an alarming increase in the number of inquiries have been recorded. From the majority of these discussions, it is apparent that athletes are being led to believe that the use of growth hormone is infinitely safer healthwise than taking anabolic steroids.

Now there is no scientific basis for this claim. Yet this myth has clearly created a tremendous interest and experimentation in the improper use of this drug. Thus far, most information indicates that the black market provides the major source of synthetic growth hormone. We have not determined, however, whether this emanates from offshore or domestic manufacturers. Accordingly, recent athlete information indicates that domestic products are indeed available.

The concern is, therefore, that synthetic growth hormone, because of its availability and perceived safety, will be used as an alternative to anabolic steroids.

Recently, Mr. Chairman, I spoke to over 2,500 high school students in an unmentioned State of your liking.

Mr. **Waxman**. It must be Indiana.

Mr. **Voy**. Particularly on this subject of anabolic steroid and substance abuse in general amongst athletes and high school students. I was surprised and dismayed at the many questions I received regarding growth hormone use. Heretofore, I had not experienced such interest, and particularly at this level of youth, in any other substance.

Growth hormone abuse in sport is certainly a health risk and constitutes, in our opinion, cheating in sport. The United States Olympic Committee is committed to guaranteeing fair competition in sport and protection of the health and welfare of our youth.

As chief medical officer of the U.S. Olympic Committee, I submit this statement before your committee and request that at least a convening of a blue ribbon committee of experts be done to investigate this situation and consider strongly placing this substance under the Federal Controlled Substance Act as a Class 2 Schedule controlled substance.

Thank you.

Mr. **Waxman**. Thank you very much, Mr. Voy. Next is Dr. Taylor.

STATEMENT OF WILLIAM N. TAYLOR

Mr. **Taylor**. Mr. Chairman, I am William Taylor, M.D., student health physician at Washington State University. I am also media spokesperson for the American College of Sports Medicine on their recent position paper for human growth hormone use and abuse in athletics.

Recently, the AMA did need to consider reclassifying human growth hormone as a Class 2 substance. Although they have not totally acted, some statements from a recent document that is entitled "Drug Abuse in Athletes: Anabolic Steroids and Human Growth Hormone." Report of the Council on Scientific Affairs, Resolution 57 and A-86, 1986.

Human growth hormone has a clear-cut application in growth hormone deficiency and other legitimate investigational uses, and also has great potential for misuse.

Another statement from this paper goes to the following: Increased availability; i.e., unlimited quantities of human growth hormone for other legitimate uses presumably would increase accessibility for illicit use.

My work with human growth hormone was really a serendipitous start. In 1981, I was studying the effects of anabolic steroids on self-using athletes, the black market, and other parameters dealing with this subject. In 1981 I discovered human growth hormone, the extracted version, being used and abused by athletes in a Florida health club. Vials with accompanying package literature were witnessed by me. The athletes wanted to know exactly what the package literature meant.

Athletes claimed a non-medical source for the drug. By the spring of 1982, I attempted to define the diversion of this particular product. At that time I was taught that the only way that you could get human growth hormone was through hospitalization, provocative studies for a slow growing child to see whether there was a growth hormone deficiency or not; X-ray studies, and entire hospital course and records sent with a prescription, written prescription to either the National Pituitary Program or two private companies.

From that point, the boards of those companies would decide whether or not there was an actual need; then the hormone would be shipped to either the pharmacy or to a physician that was administering the growth hormone for a child.

So that is a very, very strict measure, and I wondered why growth hormone was being black marketed. There seemed to be no way. That was a very strict control measure.

I attempted to find out what the diversion was like. I sent bogus prescriptions as a medical intern for human growth hormone to the National Hormone and Pituitary Association and two private companies which supplied the growth hormone. Boxes of the growth hormone came on a monthly basis from the private companies. I destroyed the growth hormone and refused further shipments. These shipments came directly to my home, and I was only a first year medical resident, not even a licensed physician.

Spring of 1982, I witnessed selling of human growth hormone, transactions among athletes and black market suppliers including mail order forms. I witnessed athletes self-using human growth hormone along with anabolic steroids by illegal diversion.

In May of 1982, I reported the use of human growth hormone to the American College of Sports Medicine at its national convention in Minneapolis.

In June of 1982, I wrote about human growth hormone abuse in athletics in my book, "Anabolic Steroids and the Athlete," and a complete chapter was on this subject.

In 1983, I began to receive letters, phone calls, visits from athletes including olympic and professional athletes who were self-using human growth hormone obtained from the black market. They sought advice on how to use it. They also requested prescriptions for human growth hormone.

Also in 1983 I began receiving letters and phone calls and visits from parents requesting the following: (A) For me to prescribe growth hormone to their adolescents for the purpose of increased heighth and athletic potential. (B) For advice on how much black market growth hormone to give their children. They had already obtained a supply of growth hormone, and they wanted to make their son or daughter a blue chipper in athletics.

I received and witnessed human growth hormone listed on black market mail order forms, directed at young athletes. I have written about human growth hormone and its abuse, and methods for control of the hormone in over a hundred medical, non-medical, and lay publications.

Spring of 1984, I attended private meetings and heard testimony from an olympic coach who claimed: "From 30 to 50 percent of my U.S. olympic athletes, both men and women, are using growth hormone because they think it works and because it is not detectable. I am also concerned about their health."

In May of 1984, I presented a paper at the American College of Sports Medicine on the abuse of growth hormone by athletes, the black market sources, and recommendation to reclassify it as a controlled substance.

In May of 1985, again more media: The NBC nightly news; Steroid Abuse and Growth Hormone Abuse.

In June of 1985, I wrote my second book, "Hormonal Manipulation," which clearly outlined the abuse potential and the use of human growth hormone by athletes. This book discussed the black market network, suggests for reclassification of human growth hormone as a Schedule II drug under the Federal Controlled Substance Act.

April 1986 I presented a paper at the University of Texas entitled, "The Case Against Human Growth Hormone Administration in Normal Children" in a day-long meeting sponsored by the University of Texas discussing abuse potential of growth hormones by athletes and adolescent athletes.

Leading pediatric endocrinologists and sports medicine physicians presented papers, and in the debate about how to control, this particular subject arose.

June 1986, I presented testimony to the AMA House of Delegates Reference Committee E to support the proposal to reclassify human growth hormone in a Class II of the Federal Substance Control Act.

October 1986, 2 years after the growth hormone is removed from the market because of slow virus disease, I presented testimony as an expert witness for the FDA against a black market steroid dealer in Florida. A significant supply, over 100 vials of Cres Cormon, the extracted version of growth hormone, was seized by police and was part of the court record.

This black market for steroids and growth hormone is part of a $100 million annual black market that is estimated by Federal agents.

In March of 1987, I witnessed black market source for synthetic Protropin, and use of such by an athlete. This particular vial looked to be the true Protropin, with the lot number etched off of the vial. The athlete claimed that the lot number would be traced back and that he would be in major trouble if the lot number on this particular vial was recorded.

Anecdotal claims by athletes today are prevalent about the synthetic Protropin on the black market.

I think, in summary, it is better to study all of the ramifications of growth hormone in a controlled setting versus self-use and social experimentation, which is what is the case with steroids.

It is difficult for anyone to fully access the steroid charisma that is afflicting our youth, and the emphasis on body image that is afflicting our youth. I support with all my efforts, courage and heart the proposal to place human growth hormone into the Class II substance. I do not see any other mechanism that I feel that will work at this time. Thank you.

[The prepared statement of Dr. Taylor follows:]

STATEMENT OF WILLIAM N. TAYLOR

INTRODUCTION

Human growth hormone has a clear therapeutic application in growth hormone deficiency and other legitimate investigational uses, and also has great potential for misuse. (1) The agent has wide abuse potential, particularly if pharmacologic benefits are shown to result from use in normal athletes (1-10) and in adolescents wishing for additional height gains for athletic or other purposes. (2-10)

Diversion of human growth hormone to the well-developed athletic black market is significant, (2-11), even though relatively strict format existed for its distribution. This format included the following:

(a) proof of need by clinical documentation to include provocative diagnostic studies during hospitalization, radiographic studies and clinical evaluation for children with growth hormone deficiency;

(b) a written prescription accompanying the clinical proof of need provided in (a) above.

Methods to control general prescription drugs with "wide abuse potential" by allowing for pharmaceutical companies to restrict their distribution in some menner have failed to date. When widespread abuse or abuse potential for a general prescription drug has been identified, appropriate control mechanisms have usually included reclassifying the drug within the Federal Control Substance Act. Amphetamines and tranquilizers, once general prescription drugs, are now controlled substances due to wide spread abuse and abuse potentials. (11)

Currently, the particulars of the diagnosis and treatment of growth hormone deficiency and relative growth hormone deficiency are points of debate among pediatric endocrinologists. And, years of investigational research are required to fully define the effectiveness and safety of human growth hormone in other illnesses. Specifically controlling the distribution of human growth hormone for legitimate uses and further investigational work would not be hampered by reclassifying it as controlled substance. It is the best method for preventing abuse by medical and nonmedical individuals.

It is my recommendation, supported by my testimony (summary to follow), that human growth hormone (all types) be reclassified in Class II of the Federal Control Substance Act.

Current AMA recommendations are being developed from the following recommendations for regulatory actions for synthetic anabolic-androgenic steroids and human growth hormone. (1) The AMA should continue to endorse current activities of the FDA, FBI, and DOJ directed toward curbing illegal distribution of these drugs. If these efforts are ineffective, the AMA should undertake a study of alternate methods of monitoring and limiting distribution. (1)

The use of HGH in normal children is an ethical problem of far-reaching proportions. (1) Increased availability (unlimited quantities) of HGH for other legitimate uses presumably would increase accessibility for illicit use. (1)

TESTIMONY OVERVIEW

1981—I discovered growth hormone (extracted) use/abuse by athletes in a Florida health club; vials with accompanying package literature were witnessed. Athletes claimed a nonmedical source for the drug.

Spring 1982—I attempted to define the diversion of HGH. I sent bogus prescriptions for HGH to the National Hormone and Pituitary program (NHPP) and two private companies (Serono and Pharmacia) supplying the hormone. Boxes of HGH came on monthly schedules from both private companies. I destroyed the growth hormone and refused further shipments. These shipments came directly to my home. I was a first-year medical resident.

Spring 1982—I witnessed HGH selling transactions among athletes and black market suppliers, including mail orders. I witnessed athletes self-using HGH along with anabolic steroids obtained by illegal diversion.

May 1982—I reported HGH use by athletes from black market sources at the American College of Sports Medicine annual meeting in Minneapolis, MN.

June 1982—I wrote about abuse of HGH by athletes and adolescents striving for athletic success in a chapter in my first book *Anabolic Steroids and the Athlete*.

1983—I received letters, phone calls and visits from athletes, including olympic and professional athletes, who were self-using HGH obtained from the black market. They usually sought advice on how to use it. Some requested prescriptions for HGH.

I received letters, phone calls and visits from *parents* requesting:

(a) for me to prescribe HGH to their adolescents for the purpose of increased height and athletic potential;

(b) advice on how much black market HGH (they had obtained a supply) to give their adolescent athletic children.

I received and witnessed HGH listed on black market mail-order materials directed at young athletes.

I have written about HGH abuse and methods for control of the hormone in over 100 medical, nonmedical and lay publications and newspapers.

Spring 1984—I attended private meetings and heard testimony from an olympic coach who claimed, "from 30-50 percent of my 1984 olympic athletes (men and women) are using HGH because they think it works and it is not detectable—I am concerned about their health."

May 1984—I presented a paper to the American College of Sports Medicine on growth hormone use and abuse by athletes, black market sources and recommendations to reclassify it as a controlled substance.

May 1985—I appeared on *NBC Nightly News* and reported abuse of HGH among athletes using anabolic steroids.

June 1985—I wrote my second book on anabolic and growth hormone abuse entitled *Hormonal Manipulation: A New Era of Monstrous Athletes*. The book discussed HGH abuse, the black market network for the hormone and suggests reclassifying HGH as a Class II drug in the Federal Controlled Substance Act.

April 1986—I presented a paper entitled: "The case against HGH administration to normal children" at a day-long meeting sponsored by the University of Texas discussing the abuse potential of HGH by athletes and adolescent athletes. Leading pediatric endocrinologists and sports medicine physicians presented papers. *The McNeil-Lehrer Report* televised portions of the meeting. A debate about reclassifying HGH as a controlled substance arose.

June 1986—I presented testimony to the AMA House of Delegates Reference Committee E to support the proposal to reclassify HGH into Class II of the Federal Controlled Substance Act.

October 1986—I presented testimony as an expert witness for the FDA against a black market anabolic hormone dealer in Florida. A significant supply of HGH was seized by police. (11)

March 1987—I have witnessed a black market source for synthetic HGH (Protropin®) and use by an athlete. Anecdotal claims by athletes are prevalent.

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Mr. WAXMAN. Thank you very much, Dr. Taylor.

Dr. Kerr.

STATEMENT OF ROBERT B. KERR

Mr. KERR. Thank you, Mr. Chairman.

Today I would like to give you some background data on growth hormone today, particularly its illegal distribution and use. Human growth hormone was found to have anabolic, or strength-enhancing qualities a few years prior to the 1984 olympic games. Eastern European block countries probably were the first to use this drug to enhance athletic qualities.

In 1982, an executive of the Kabi Corporation, the manufacturers of the human growth hormone Cres Corman, told me that to his knowledge, 100 percent of the human growth hormone being imported into East Germany was being used by athletes. To his knowledge, he said: "Not a drop was being used in needy children."

Bodybuilders in the United States and Canada were probably the first of our athletes to use growth hormone, as it was being sold rather extensively at that time on the black market; but human growth hormone at that time had a competitor that was being sold just as extensively, and that was a monkey growth hormone. The product was being processed in this country by marginal laboratories, and was promoted to bodybuilders and weight lifters as gorilla hormone.

It appears at this time there is no effective way to halt black market activities in these anabolic drugs. Recent FDA and FBI prosecutions of drug dealers is a start, but it is not more than just a drop in the bucket. I reported a number of dealers to FDA and other law enforcement agencies, and most of these people I found are back on the street, plying their trade, and that the laws obviously are just not strict enough.

I have been asked before if there is a connection between the black market dealers and organized crime, but it appears to me that the illicit dealers are not organized, and are individuals who are practically alone, and therefore might be more easily dissuaded from their activities if the laws become more rigid and the penalties more severe.

When you consider that practically every weight training facility in this country has an employee or a client who trains there, or someone who simply stops by now and then to sell illicit anabolic hormones, and when you consider how many millions of men and women are now buying these products in the United States, it is a wonder that organized crime is not interested in their business.

By the 1984 olympic games in Los Angeles, human growth hormone was always the topic of conversation between athletes and coaches, no matter what country. It apparently was used by a rather unexpectedly high percentage of athletes, and as far as the types of athletes, I must say that in weight athletes, it is not as common these days as in the sprinting athletes, the field-eventers.

The brand name of the human growth hormones at that time were Asellcarin and Cres Corman. By that time, only an unenlightened few body builders were still turning to the simeon growth hormone, but it is still available today for those who desire it.

The size of the drug sales by independent dealers, anabolic hormones, growth hormones and other prescription drugs were and still are sold by mail order dealers, flyers, catalogs and other sheets that are sent to athletes throughout the country, and I have some examples of these that I will be I will be happy to leave. There are also some underground newsletters to athletes, describing how to use their black market drugs.

But you will find human growth hormone, you will find monkey hormone as well. I have sent copies of these in the past to the DEA, the FDA, and others; and hopefully these examples are now out of business, but I have been assured that new businesses crop up practically every week.

When you have one of these mail order catalogs, all you do is fill out the order form for the desired drugs, and include a check. It is just as simple as that. One of these says, "Not for sale to minors," but nowhere does it ask for the buyer's age or proof of age. Another says, "Not for sale where prohibited by law." That must be just about everywhere.

Some dealers simply drop by the various gyms with suitcases full of these drugs, or they sell them out of the back of their car. It is a very common thing. If you want to find out about it, just simply go to your local gym.

There have been many people with whom I have spoken who have been sold fraudulent anabolic hormones, including growth hormone.

I have here a sealed container of Asellcarin, a brand of human growth hormone, which was sent to me, which was bought by a black market dealer and sent to me by an athlete from the Midwestern United States. He said he paid $300 a vial for three vials. When he did not receive the muscular gains expected from the first vial and a half, he had some of the material examined and was told that the vial contained nothing but water.

When he examined this third, sealed vial, there was a noticeable tiny hole drilled in the top. Now, you see the cover is still there; it is still unsealed. There is a tiny hole. And this was covered by metallic cement of some sort, so that you really could not see it unless you examined it carefully.

I assume that someone drilled this tiny hole and then withdrew the Acellorin with a hypodermic syringe, a needle, and filled the vial with water or some other fluid. One might wonder if the fluid was even sterile.

I received letters from others asking if growth hormones were blue in color. Others have written that they doubted the authenticity of their illicit hormones for other reasons. So some of these cases were simply con games, perpetrated on unwise individuals.

Again, we might wonder if the substituted substances were dangerous in any way.

Last summer was I was invited to the University of Texas to take part in a day-long seminar on the growth hormones. The topic selected for me was the athletic use of these drugs. The speakers varied widely in their expertise and locale, and just prior to the seminar it was announced that the recombinant growth hormone would soon be released by the Genentech company.

Dr. Ann JoHanson represented Genentech at that meeting. I told her and the audience that I predicted that within weeks after the release of Protropin it would be available by some means on the black market. Now I have been told that my guess was not off.

Athletes have told me that they bought Protropin on the black market by mid-summer, and it has been available ever since.

I reported this in a letter to Dr. JoHanson this winter, and I believe that she found this news to be something that she had not heard before. I have included copies of my letters to Dr. JoHanson and her letters to me.

Just prior to notifying Dr. Johanson of the prevalence of this source of the drug, I wrote to Dr. Robert Boyd of the United States Olympic Committee, notifying him of the availability of the Protropin drug. Later he asked me if I would be interested in addressing your committee today.

At that time, we both thought that it might be interesting to show you how available Protropin is by buying some from the black market. It perhaps would also show some light by perhaps introducing some serial numbers or some other means of tracing its source from Genentech. Dr. Voy and I were each going to buy a container of Protropin until we found out that its cost was $450. So I suggested to Dr. Voy that I would buy the product, which contains two vials of 10 ccs each, and I would donate a vial to him.

Now that I think about it, I do not think it is tax-deductible.

At any rate, I have got a vial of it here, and it is open for your investigation.

Let me give you a little background. I have made friends with athletes from all over the world, throughout the years, and I have generally gained ideas on who dealt in these types of drugs. But when I went to buy this, I felt that if I went to a known dealer, that might be just a little too easy, so I simply chose a bodybuilder in Southern California who I had known in the past had taken anabolic drugs from the black market.

One call did the trick. I received the package of Protropin one week later, and paid him the $450. I do not believe that this fellow has ever sold drugs before, but I was certain that he knew from whom to buy.

So you can see how quite easy it is to purchase this drug, no matter what Genentech says.

There are a couple of important issues here. The bodybuilder from whom I bought the drug said a friend of his works for Genentech and was giving me the drug at the wholesale cost. Selling out the back door, huh? This is a very depictable ploy and I have heard it so many times before. Everyone who ever sold human growth hormone before, or now with Protropin, always says that the dealer was his brother who works for the company, or an uncle, or that the brother is a pharmacist or some other type of friend or relative. You always hear that same excuse.

One week ago I spoke to an olympic weight lifter from San Jose, CA, who just bought two containers of Protropin, and when I asked his friend's name, he declined. Perhaps he felt embarrassed in admitting to me that he had dealt with an illegal drug source. He simply said that he bought it from an employee of Genentech. I am certain that Genentech is above all of this business; but it certainly is besmirching their name, and I would suggest for the sake of scandal that Genentech might undertake an internal investigation into this matter of this product being sold.

I think my time is up. I'll skip the rest.

At any rate, I have a lot of material here that you might find interesting.

[Testimony resumes on p. 110.]

[The prepared statement of Mr. Kerr follows:]

Robert B. Kerr, M.D.
316 East Las Tunas Drive
San Gabriel, CA 91776
(213) 285-1154

Gentlemen:

I would like to give you some background data on growth hormone today, particularly its illegal distribution and use.

Human growth hormone was found to have anabolic (or strength-enhancing) qualities a few years ago, a few years prior to the 1984 Olympic Games. Eastern European bloc countries probably were the first to use this drug to enhance athletic qualities. In 1982, an executive of the Kabi Corporation, the manufacturers of human growth Crescormon, told me that to his knowledge, 100% of the human growth hormone being imported into East Germany was being used by athletes! To his knowledge, he said, not a drop was being used in needy children!

Bodybuilders in the United States and Canada were probably the first of our athletes to use growth hormone as it was being sold rather extensively at that time on the black market. But, human growth hormone had a competitor that was being sold just as extensively, and that was monkey growth hormone. This product was being processed in this country by marginal laboratories and was promoted to bodybuilders and weight-lifters as "gorilla hormone."

At that time, quite a number of physicians around the country tried to steer the athletes away from the black market by prescribing the human growth hormone to worthy athletes. But, to "legalize" the use of growth hormone, or any other anabolic drug for that matter, in this manner, is a fruitless endeavor indeed. Athletes, and I'm not speaking particularly of the track and field athletes, but more commonly those in bodybuilding and power-lifting, who desired not only greater strength, but a greater body mass, would (and will) simply take a prescribed medication and supplement that with whatever else they can buy on the black market. I believe now that this type of control of the medication is frought with failure. There is simply, at this time, no way to effectively halt the black market activities. Recent FDA and FBI prosecutions of drug dealers is a start, but it's still no more than a drop in the bucket. I reported a number of dealers to the FDA and other law enforcement agencies but most are back on the street at this time, plying their trade. The laws are just not strict enough.

I've been asked before if there's a connection between the black market dealers and organized crime. It appears to me that the illicit dealers are not organized and are individuals who are practically alone, and therefore, might be more easily dissuaded from their activities if the laws become more rigid and the penalties more severe.

When you consider that practically every weight training facility in this country has an employee or a client who trains there, or someone who simply stops by now and then, who is selling illicit anabolic drugs-when you consider how many millions of men and women are now buying these products in the United States, it's a wonder that organized crime isn't interested in their business.

There is a gym in a Los Angeles suburb that I've always thought of as "drug free" and I've used it as an example in the past when speaking to others about this problem. Last week I was told that every Friday night a dealer in illicit hormones makes a delivery to a manager of that gym. So, I guess that I've been disillusioned more than once, and at this time, I've yet to hear of a gym where this activity is not found!

By the 1984 Olympic Games in Los Angeles human growth hormone was always the topic of conversation between athletes and coaches, and it apparently was used by a rather unexpectedly high percentage of athletes. The brand name of the human growth hormones were Ascellacrin and Crescormon. By that time, only an unelightened few bodybuilders were still turning to the simian growth hormone, but it was, and still is, available to those desiring it.

Besides the drug sales by independent dealers, anabolic hormones, growth hormones and other prescription drugs were, and still are, sold by mail order dealers. Flyers, catalogues and order sheets were sent to athletes throughout the country by the mail. I have examples of some of these mailers with me today. I've sent copies to the DEA, the FDA and others, and hopefully, these examples are now out of business. But I understand that this type of business is still flourishing. With these you simply fill out the order form for the desired drugs and include a check, it's as simple as that! One of these says, "Not for sale to minors," but it fails to ask the buyer's age or proof of age for that matter. Another says, "Not for sale where probibited by law"-well, that must be just about everywhere! Some dealers simply drop by various gyms with suitcases full of drugs for sale or they sell them out of the back of their cars.

There have been people with whom I've spoken who were sold fradulent anabolic hormones, including growth hormone. I have here a sealed container of Ascellacrin, a brand of human growth hormone, which was bought from a black market dealer by an athlete from the midwestern United States. He said that he paid $300.00 a vial for three vials. When he did not receive the muscular gains he expected from the first vial and a half, he had some of the material examined and he was told that the vial contained nothing but water! When he examined this third, sealed vial, there was a tiny hole, that you'll notice, through the seal which was covered by a small amount of metallic cement. I assume that someone drilled a tiny hole through the metal cap and seal, withdrew the Ascellacrin with a hypodermic syringe and needle, then filled the vial with water or some other clear fluid before filling in the hole. We might wonder if the fluid was even sterile!

I've received letters from some asking if growth hormone was blue in color. Others have written that they doubted the authenticity of their illicit hormones for other reasons. So, some of these cases were simply con games perpetrated on unwise individuals. Again, we might wonder if these substituted substances were dangerous in any way.

I've been told that the monkey growth hormone is still for sale, and you'll see it in the illicit drug catalogues that I have here today, and you'll see that it's nearly as expensive as the other types of drug hormone.

Last summer I was invited by the University of Texas to take part in a day-long seminar on the growth hormones. The topic selected for me was the athletic uses of this drug. The speakers varied widely in expertise and locale. Just prior to this seminar it was announced that the recombinant growth hormone would soon be released by the Genentech Company. Doctor Ann Johanson represented Genentech at that meeting, and I was impressed by her. I told her, and the audience, that I would predict that within weeks after the release of Protropin, it would be available by some means on the black market. I've been told that my guess was not far off. Athletes have told me that they bought Protropin on the black market by mid-summer and it's been available ever since!

I reported this in a letter to Doctor Johanson this winter, and I believe that she found this news to be something that she had not heard before. I've included copies of my letters to Doctor Johanson and her letter to me. Just prior to notifying Doctor Johanson of the prevalence of this illegal source of the drug, I wrote to Doctor Robert Voy, the Medical Director of the United States Olympic Committee, notifying him of the availability of this Protropin drug. Later, he asked

BEST COPY AVAILABLE

me if I would be interested in addressing your committee today, and at that time, we both thought that perhaps it might be interesting to show you how available Protropin is-by buying some from a black market source; it perhaps would also shed light by showing a possible serial number or some other means of tracing its sources from Genentech. Doctor Voy and I were each going to buy a container of Protropin, until I found out that its cost was $450.00. So I suggested to Doctor Voy that I would buy the product, which contained two vials of 10 ccs. each, and I would donate a vial of that to him. Now that I think about it-I don't think that it's tax deductible!

Throughout the years, I've made and kept friendships with quite a number of athletes throughout the world-including the Soviet countries. This has gained me knowledge about illicit drug dealers, many of whom I've reported to federal agencies. But, in buying the Protropin, buying from a known dealer was too easy, so I chose simply a bodybuilder who I knew to have taken black market anabolics in the past. One phone call did the trick-I received the package of Protropin one week later and I paid him the $450.00. I don't believe that this fellow has ever sold drugs before, but I was certain that he knew from whom to buy. So you can see that it's really quite easy to purchase this drug no matter what Genentech says!

This bodybuilder from whom I bought the drug said that a friend of his works for Genentech and was giving me the drug at the wholesale cost! This is a very predictable ploy-I've heard this so many times before. Everyone who sold human growth hormone before, or now with the Protropin, always says that the dealer was his brother who works for the company, or an uncle, or that the brother is a pharmacist, or some type of friend or relative. It's always the same excuse. One week ago I spoke with an Olympic weight-lifter from San Jose, California who had just bought two containers of Protropin "from a friend who works for Genentech in San Francisco." I asked his friend's name, but he declined. Perhaps he felt embarrassed in admitting to me that he had dealt with an illegal drug dealer, and yet again, perhaps, a Genentech employee had a better sound to it!

Now, I'm certain that Genentech is a very reliable and sound company, and I doubt very much that they would have anything to do with selling their product from the back door. Though I would suggest for the sake of scandal that Genentech undertake an internal investigation into this matter. With the prevalence of their product on the black market throughout this country, apparently a large amount of Protropin is missing from hospital pharmacies or wholesalers' inventories somewhere. Someone is making alot of money on these sales,

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and it's all untaxable!

Doctor Terry Todd, of the University of Texas, told me a few weeks ago that a boxcar with Protropin within it was hijacked from an eastern freight yard, and was probably the source for this Protropin. But, you know, I've heard that same exact story, word for word, given in past years to explain why human growth hormone was on the black market. Now, either there's a drastically unguarded freight yard in the east that's had a high number of freight cars missing, or it's a fallacy perpetrated by those who wish to cover up their own corruption. I suspect with the high retail cost of Protropin, plus the thousands of buyers, someone, hopefully after leaving Genentech, is supplying the black market with their own inventory. Perhaps I'm wrong about this, but I wouldn't think it too difficult to check it out-Genentech could certainly ask their customers, physicians, pharmacies and wholesalers to critically identify their sales. If the Lilly Company offers its recombinant growth hormone for sale, they might also be confronted by this same sham.

If laws are enacted, and Protropin and any other growth hormone is eliminated from the black market, does that mean that athletes will return to the simian growth hormone-hopefully not! But with the millions of people, men and women, in this country and Canada who are determined to take something to enhance their strength or size or whatever, I'm certain that some form of growth hormone will be available, perhaps from European manufacturers, but hopefully, the FDA and other agencies will be able to cope with this problem. But these and other problems might confront your committee some day in the future.

Today in bodybuilding gyms throughout the country the most sought after anabolics are the exotics. This includes East European anabolics that are smuggled into this country, and the FDA and the FBI seem to be curtailing alot of this traffic. But just as commonly found are the veterinary products-Winstrol V and Equipoise (I believe that Equipoise was the name of a derby winner in the 1930's, and that certainly gives you confidence in the medication, doesn't it?)! These products are said to be sold by veterinarians, but I don't know ~~that~~ this is true, but certainly some veterinary source is at work here.

I reported to the FDA a clinic in San Jose, California that develops designer anabolics for their clients. I've been told that the owner is not a physician or a chemist, and he's been arrested before for selling these drugs. So, obviously there are some laws that need amending.

Now to get to a touchy aspect of growth hormone. Through the media, we've all heard stories of parents wanting to obtain these drugs so that their young teenage sons (and perhaps, daughters) can grow past their expected height and satisfy some parents' hopes. Unfortunately, it's true to a certain extent. I don't know what the numbers are-but I, and other physicians with whom I've spoken, have been approached by a few such parents. If I couldn't dissuade them from this expensive, and no doubt futile experiment, I then referred them to a pediatric endocrinologist, knowing full well that they would be turned away. I wonder how many of these simply turned to a black market source for their growth hormone. The idea of wanting the best for your children is an idea that we all share, but this is a disillusion, and I don't expect any of these teenagers who are potentially deemed short statured to become an NBA or an NFL giant. This is wishful thinking. I'm afraid that some of my physician colleagues can be counted in the ranks of these parents. A law controlling these drugs will discourage such parents.

I don't believe that such laws will abolish anabolic drug usage in athletics. A Russian athlete last week told me "it's a fact of life, as long as there is athletics, there'll be anabolic hormones." Athletes are going to take anabolic hormones-it's just the way it is. Now, someday an anabolic process that doesn't entail medicines will give these athletes their strength and size, but until then, it's a way of life. There are on the horizon new methods that could pave the way to this drug-free athletics.

But, the bottom line to all of this is simply this-whether the drugs are leaked to the black market from pharmaceutical wholesalers, smuggled in from Mexico or some other country or whether the drug is manufactured in someone's kitchen in Anaheim, California, it's all illegal and untaxable. If I have to pay taxes, how come these dealers do not?!?! The FDA and the FBI are doing any exemplary job. But if we don't give them the laws to stop these illegal processes, the practice will only escalate.

Thank you!

information newsletter

UNDERGROUND STEROID HANDBOOK UPDATE #1: HUMAN GROWTH HORMONE

The USH UPDATE is a bimonthly publication. In these bulletins we will point out and correct any errors we may have made in the original UNDERGROUND STEROID HANDBOOK. Also, we will inform you of any new drug developments in the realm of competitive bodybuilding and powerlifting. This is our first issue and we will address ourselves to what we think is the biggest blooper we made in the USH, our altogether too cursory examination of Growth Hormone.

We find that Growth Hormone is the most expensive, most fashionable, and least understood of the new athletic drugs. It has firmly established itself in powerlifting and within a few years will be a commonly used drug in all strength athletics. We are discussing in this report only one type of growth hormone, Asellacrin by Serono Labs. This is Human Growth Hormone. It comes in four bottles to a box, 10 IU's to a bottle. The bottles contain an unreconstitoted whitish powder, with biostatic water (5 cc's per bottle) to be added. The biostatic water is not part of the four bottle package. People familiar with Pregnyll (HCG) will find Asellacrin packaged similarly. Once reconstituted, the GH must be refrigerated. Serono's wholesale price to pharmacies is $600 per four bottle box. They offer lower wholesale prices to quantity buyers.

Most of the information available about GH in the past was on the effects of Rhesus Monkey Growth Hormone. All the bad side effects such as acromegaly (thickening of the bones) and diabetes have now been determined to be mostly from the inferior monkey hormone. Human Growth Hormone reconstitutes into a clear liquid. The Rhesus hormone is brownish. Asellacrin is extracted from the pituitaries of human cadavers. It is not 100% pure GH, as there are traces of other chemicals and hormones found in the pituitary.

Just why is it such a desired drug? It works differently than anabolic steroids. Not only does it make muscle cells grow bigger, but it makes the body grow more muscle cells. It also makes the rest of the body grow. Tendons and ligaments get thicker, as do bones (if you are still able to grow heightwise, you will grow taller). You might surmise why powerlifters have taken a shine to it. Champion powerlifters get many injuries because usually their muscles are stronger than their bones, ligaments, joints and tendons. GH will allow growth of these weak links. Also, GH mobilizes stored fat, so that it is metabolized at a faster rate than normal. It does not interfere with the reproductive systems of either men or women. Receptor sites on the cells are not the same as steroid receptor sites, so if you have plateaued on anabolics, your body can still respond to Growth Hormone. And lastly, it is not detectable in drug tests used in international Olympic and Powerlifting competitions.

Most everyone produces some Growth Hormone naturally. The highest amounts are released by the pituitary during the first few hours of sleep. It was also thought that GH was released in response to highly stressful anaerobic exercise, but the most recent studies find this to be true only in people up to the age of about thirty. As we mentioned, GH makes many things grow in the body and we have found the most significant benefits of it (health-wise) is in its ability to keep the thymus gland large. The thymus gland is a major gland that is part of the immune system. It produces antibodies which fight potential disease and infections and generally keep the body healthy, young appearing and well. If the thymus gland reduces in size, your immune ability will be lessened. Two major factors cause the thymus gland to shrink. The first is the reduction of the body's output of Growth Hormone after the age of thirty (ahah!). And the second is anabolic steroids. In fact, the major th hazard of anabolic steroids is their ability to reduce thymus size, thus limiting your body's antibody output. We've encountered many steroid users who start the drugs and immediately come down with a cold or flu-like symptoms. Now you know the reason. Of course, you can boost your own natural output of GH with arginine, ornithine, vasopressin, bromocriptine, and L-DOPA supplementation (we do). But the amout of GH you can inject is comparitively huge to the trickle that the pituitary can put out even in the most elevated way.

Let's discuss how GH is used by the body once it is in the bloodstream. GH is activated by enzyme-like chemicals called somatomedin. Somatomedin helps GH mediate its effects. Once GH is in the bloodstream, it saturates the available somatomedin in about twenty minutes. In this state, the half life of the GH is forty eight hours. If there is not enough somatomedin available to activate the GH, its half life in this unsaturated state is about half an hour. We know no way of increasing somatomedin synthesis. Growth Hormone reduces insulin's ability to put glucose in the cells. Also, strangely enough,, GH increases insulin levels in the body.

We've seen many people who have not had good results in using Growth Hormone. Here are some reasons why GH won't work in those people:. GH won't increase body size without sufficient calories. We've seen more success of GH used by powerlifters as opposed to bodybuilders because possibly, powerlifters are not afraid to eat. A few people manufacture antibodies to the Growth Hormone, rendering it useless. Many studies show that GH works best in an environment high in androgens and low in estrogens and cortisone. Most athletes don't use a high enough dosage.

There has never been any recommended dosages published (especially for athletes). Most everyone we've seen, powerlifters and bodybuilders both, use two IU's every forty eight hours for as long as their money holds out. Some have mixed the GH with testosterone aqueous to insure high androgen levels. Also, when GH has been used while the person has been on steroids for a long duration, we've seen estrogen antagonists such as Nolvadex or Teslac added to control the estrogen resulting from aromatization.

Most people will not feel the effects of GH blocking insulin's ability to load glucose into the cells because of the higher insulin levels also ncountered. For those that do (and the noticable effects will be loss of strength and a flat, depleted look to the muscles) the easiest way to combat this is to stay off GH for a few days when they begin to notice the lack of energy and then to load carbohydrates into the body. We discuss carbohydrate loading in the ULTIMATE DIETING HANDBOOK. Some people are supplementing their insulin with injectable forms. Most people, doctors included, don't know how to do this properly. They assume that insulin should be increased in a linear level compared to the elevated blood sugar levels. This is not true. A mathematical formula of normal insulin value/normal blood sugar level = new insulin value x)/elevated blood sugar level is invalid. The proper (x) value cannot e found mathematically. We don't know how to find it accurately.

People who take large dosages of GH, in the 5 IU's and up per 48 hours ange (and we personally find this to be the minimum amount that will elp athletes) usually inject all the GH at once, compromising the GH's bility to saturate the available somatomedin. A more logical dministration would split the amount injected over a period of a few ours.

We'd like to give your our personal observations about GH. We think that it is quite a safe drug. Most of the side effects are either heresay or were related to the inferior rhesus-derived Growth Hormone. We think that it is an athletically beneficial drug for both men and women. We find that it works when taken in large dosages over a long enough duration. Most people cannot afford the cost of this therapy. Very soon, in a matter of months, GH will be available at a vastly reduced price because it is now a genetically engineered drug. That is to say that scientists have invented certain strains of bacteria to produce Growth Hormone in its human form. This was first done at Baylor Medical school, but many places are doing it now. Because this new way of producing GH does not involve dissecting cadavers and extracting the substance from the pituitary, it will not only go down in price, but up in availability. We also predict that once this happens, you will see many non-athletic people, at first in Europe away from FDA influence, use this drug as a life and youth extender, as its properties of keeping the thymus enlarged are already well known.

Here is the forecast of what we will be talking about in upcoming UPDATEs. We will be analyzing the new generic Dianabols now that Ciba has withdrawn that drug from the world market. We'll be featuring reports on two new exciting injectables, Equipoise and Anatropin. A comparative study of the different brands of needles and syringes is under way, giving you the results of the Painless 22 Gauge Shootout. We'll discuss the oil/water partitions of the various injectables, which tell you how long it takes for a shot to really get working. We will rereview the testosterones and how they relate to powerlifting. Injectable Winstrol is getting a lot of excitement lately, so we'll have a go at that subject. Of course, we're always open to suggestions.

A few of you might balk at the $2 price we charge for our Updates. As you can imagine, ours is a limited readership. What you cannot imagine is the enormous cost there is to us in finding out all this information. We don't want to tell you how much we paid out for Growth Hormone, suffice to say that the amount could also buy you a VERY nice motorcycle or a cheap shit box car. If you have read our USH (and we assume that you have) you know that we always try to save you money.

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ROBERT B. KERR, M.D.
GUILLERMO A. LAICH, M.D., Ph.D.

BIOMEDICAL AND SCIENTIFIC DEVELOPMENTAL
SYSTEMS FOR HIGH PERFORMANCE ATHLETES
HUMAN PERFORMANCE
SPORTS MEDICINE
BIOMECHANICS

February 17, 1987

Genentech Company
460 Point San Bruno Boulevard
South San Francisco, California 94080

Attention: Ann Johanson, M.D.
Director of Medical Affairs

Dear Doctor Johanson:

I had the privilege of speaking with you at the symposium last April at the University of Texas on the topic of human growth hormone.

You might recall that I was the speaker discussing the athletic uses of the human growth hormone.

At that time, I mentioned to you that I was concerned that your product might become available through black market sources, and such is now the case. I've heard from coaches, athletes and trainers throughout the country and Canada who say that the Genentech growth hormone is readily available through black market sources throughout the hemisphere. I've also heard from people in Western Europe who say that they are obtaining it there also via black market sources. It seems that there is a wealth of the material for sale. I gather that it is being sold for around $300.00 for ten or so units.

I thought that this should be brought to your attention because you never know when some investigative reporter might learn how readily obtainable your product is on the black market, and develop some sensationalism about the whole thing, and I certainly wouldn't want that type of advertising to be used against *you*

I have not heard where the black market sources obtain the product, whether it is from somebody at Genentech or whether it is a wholesaler or distributor whatever, but perhaps, you might be able to investigate this situation and find a remedy for it.

If I can be of any further assistance to you, please don't hesitate in contacting me.

My very best,

Robt. Kerr MD

Robert B. Kerr, M.D.

Genentech, Inc.

March 12, 1987

Robert B. Kerr, M.D.
Biomedical and Scientific Developmental
  Systems for High Performance Athletes
316 East Las Tunas Drive
San Gabriel, CA 91776

Dear Dr. Kerr,

Thank you for your letter of February 17, 1987. Your concern about the potential misuse of Genentech's Protropin^{R} human growth hormone is, of course, a significant concern of ours. As you know, Genentech has taken great measures to control the distribution of Protropin to guard against misuse. In fact, Protropin is only available from hospital pharmacies where there are qualified doctors who treat short children diagnosed as growth hormone deficient, and through Home Health Care of America where each individual prescription is scrutinized and screened for appropriate indication.

Genentech's distribution system goes beyond that which even FDA has authority to require. We take pride in our product and we also take appropriate precautions.

Although you suggest that Genentech's product is widely available on the black market, Genentech has no obtained evidence of illegal distribution of Protropin. Moreover, we have agreed to provide any evidence of diversion voluntarily to the FDA and the Department of Justice. Consequently, we appreciate your concern and will forward your inquiry to the appropriate federal officials for investigation. Any hard evidence that you have that Protropin is being diverted for unlabeled uses should be given to those agencies.

Once again, we share your concern. Thank you for bringing it to Genentech's attention.

Sincerely,

Ann J. Johnson, M.D.
Associate Director
Medical Affairs

ROBERT B. KERR, M.D.
GUILLERMO A. LAICH, M.D., Ph.D.

BIOMEDICAL AND SCIENTIFIC DEVELOPMENTAL
SYSTEMS FOR HIGH PERFORMANCE ATHLETES
HUMAN PERFORMANCE
SPORTS MEDICINE
BIOMECHANICS

March 17, 1987

Ann J. Johanson, M.D.
Associate Director
Medical Affairs
Genentech, Inc.
460 Point San Bruno Blvd.
South San Francisco, California 94080

Dear Doctor Johanson:

Thank you for your letter of March 12th. I do not think that you really know the degree that Protropin has invaded the black market activities in this country and in Canada, but I recently purchased a vial of Protropin from a black market dealer to prove how easy it was.

I have also been asked by Doctor Robert Voy, of the United States Olympic Committee, if I could purchase a vial for him so that he also could verify how easy it is to obtain this drug.

I know of probably at least then or twelve black market dealers that I have heard of through the grapevine who can supply your company's product at any time.

Doctor Voy recently asked me if I would be interested in testifying before a United States Senate Subcommittee hearing that will place under a triplicate registration and, of course, that is obviously one step towards regulating this, but someone is making a vast amount of money by selling this on the black market.

Now, one possibility is a comment that I heard from Doctor Terry Todd, of the University of Texas, who stated to me that he had heard that a "boxcar shipment" of Protropin was supposedly damaged in transit in the eastern United States, but instead was taken and sold to black market dealers, I don't know if this is just an anecdotal comment or that there is some truthfulness to it.

It would appear to me, from all of the gossip that I have heard from atheletes, that probably the widest use of this drug right now is through the black market. I've hardly talked to a soul throughout this country and Canada who has not had the opportunity to purchase Protropin from any number of dealers. And, of course, I mean black market dealers.

The vial of Protropin that I bought, I threw away in the trash, as I certainly had no use for it, but is there an identification number of some sort on the container that could more readily identify its source? If so, please let me know and when I purchase a vial for Doctor Voy we will look and see if there is such a distinguishing mark on the vial. And, of course, if I can be of any further information to you on this topic, I will be happy to help in any way that I can.

My very best wishes,

Robert B. Kerr, M.D.

RBKclh

Genentech, Inc.

April 2, 1987

Robert B. Kerr, M.D.
Biomedical and Scientific Developmental
Systems for High Performance Athletes
316 East Las Tunas Drive
San Gabriel, California 91776

Dear Dr. Kerr:

Thank you for your letter of March 17, 1987 to Dr. Johanson. We are referring it to the appropriate federal officials for further investigation. We have agreed to cooperate with them in any way that we can. If you have any further information regarding the alleged misuse of Protropin (somatrem for injection), please send it to me directly. We appreciate and share your concern.

Sincerely,

Patricia J. Kenney

Patricia J. Kenney
Senior Corporate Counsel

cc: John Fleder, Esquire
Chief, Office of Consumer Litigation
United States Department of Justice
Washington, D.C. 20857

Daniel L. Michels
Director, Office of Compliance
Room 260 MPN HFN-300
5600 Fishers Lane
Rockville, Maryland 20530

Catalog

From [redacted]

AUGUST'83

NEW ITEMS

Bolasterone(Tes-10)	30ml@7mg	$225.00
Dyhydrolone(Tes-20)	30ml@20mg	$300.00
Dymethyzine(Tes-30)	30ml@16mg	$400.00
→ Rheses Monkey Hormone	10ml	$200.00

ORALS

Dianabol(Methandrostenolone)	100@5mg	$25.00
Anavar(Oxandrolone)	100@2.5mg	$30.00
Winstrol(Stanozolol)	100@2mg	$19.00
Maxibolin(Ethyestranol)	100@2mg	$24.00
Anadrol-50(xymetholone)	100@50mg	$72.00
Methylestosterone Linguets	100@10mg	$12.00
	1000@10mg	$16.00
Levodopa(Dopar)	100@250mg	$25.00
Trisoralen(Trioxsalen)	28@5mg	$28.00
Proloid(Thyroglobulin)	100@1.5gr	$12.00
Nolvadex(Tamoxifen Citrate)	60@10mg	$52.00
Halotestin(Android-F)	60@10mg	$52.00
Efedrin Sulfhate	1000@.375gr	$34.00
Aldactazide	100@25mg	$15.00

INJECTABLES

Testosterones

Cypionate	10cc@200mg	$16.00
Enanthate	10cc@100mg	$16.00
Propionate	10cc@100mg	$16.00

Aqueous Suspension	10cc@100mg	$12.00
Methandroil Dipropinate(Therobolin)	10cc@50mg	$12.00
Durabolin(Nandrolone Phenpropionate)	2cc@50mg	$6.60
Equipoise(Boldenone Undecylenate)	10cc@50mg	$46.00
	50cc@50mg	$145.00
Winstrol-V(Stanozolol)	10cc@50mg	$46.00
	30cc@50mg	$75.00
Epinethrine	30cc@100mg	$20.00
Wydase(Hyaluronidase)	10ml@150IU	$20.00
Human Chorionic Gonadrotropin	10ml@10,000IU	$15.00
	10ml@20,000IU	$30.00
→ Crescormon(Somatropin)	1 vial@ 4 IU	$100.00
→ Assellacrin(Somatropin)	1 vial@ 10 IU	$600.00

Deca-Durabolin-(NANDROLONE DIPROPINATE) - $10.00

MEXICAN

Sostenon 250(with needle)	1cc@250mg	$10.00
Primoteston Depot	1cc@250mg	$6.00
Primbolan	30@5mg	$10.00
Primobolan Depot	1cc@50mg	$10.00
Anatropin	1cc@100mg	$10.00
Dianabol(Methandrostenolone)	10cc@25mg	$25.00
	50cc@25mg	$65.00

MISCELLANEOUS

Cheque Drops(Mibolerone)	55ml@100mcg	$27.00

Syringes

20 Gauge	3cc	1½	.30ea.
22 Gauge	3cc	1½	
25 Gauge	3cc	5/8	

B-12(Cyanocobalamin)	30ml@1000mcg	$10.00
B-Complex	30ml@1000mcg	$8.00
Liver	10ml@20mcg	$8.00

EUROPEAN

Orals

Nilevar(Nesterolone)	30@10mg	$19.00
Proviron(Nesterolone)	20@25mg	$19.00
Cynomel(Liothyronine)	30@25mcg	$10.00
Primobolan(Metenolone)	30@5mg	$9.00
Praxilene(Naftidrofuryl)	20@200mg	$15.00
Tricana(Triiodothyronnie)	100@125mg	$23.00

INJECTABLES

Primobolan Acetate(Metenolone)	Box of 3 1 ml@20mg	$15.00
Primobolan Depot(Metenolone)	Box of 3 1 ml@100mg	$27.00
Parabolan(Trenbolone)	Box of 2 1.5ml@76mg	$16.00
Trophobolene(Androgen&Estrogen)	1ml@80mg 80	$17.00

SPECIAL UPDATE

DYHYDROLONE & DYMYTHYZINE
(TES-20 & TES-30)

The following two anabolic steroids are included in the same family of the new advanced generation chemicals originating in East Germany. It is common knowledge in the sports world that the eastern bloc countries, e.g. the Soviet Union and East Germany, have for many years developed and administered anabolic steroids to their competing athletes. Many Americans feel that this research has given the eastern bloc an unfair advantage over their peers, especially in strength and muscle oriented sports.

* **DYHYDROLONE (TES-20)** .... 30 ml @ 20 mg

Dyhydrolone is being hailed in the United States as a major breakthrough for use by powerlifters. Its potential strength gains surpass any other anabolic steroid available in the free world today. Through its use a powerlifter should expect to amass at least 20 pounds of bodyweight within 2 weeks. Accompanying this size will be some water retention, so it is recommended that the powerlifter use 1 Proviron tablet daily, thereby minimizing this side effect.

The Net Nitrogen Retention (NNR) of Dyhydrolone is the highest available of any anabolic steroid designed for powerlifters (the NNR of Mythytestosterone is 100/100, Bolasterone [Tes-20] is 2800/2135):

Component #1	4000/500
Component #2	2200/300
Component #3	1000/1000
Component #4	500/20
Total NNR	7700/1820

9

Administration: 20 mg per day.
Delivery: 22 gauge syringe intramuscularly
Duration: 4-6 week cycle; a minimum 4 week off-cycle
Storage: Refrigerate 36° to 46°
Testing: SMA-25, Chem Profile every cycle

5

DYMETHYZINE (TES-30) .... 30 ml @ 16 mg

Dymethyzine is the most outstanding anabolic steroid ever benefited by bodybuilders. It is the only chemical so high in Net Nitrogen Retention (NNR) that it actually alters the RNA/DNA predetermined muscle fiber plasia (a hyperplasia inducing agent)!

Component #1	4000/2000
Component #2	2300/6500
Component #3	10000/7500
Component #4	1200/100
Total NNR	17500/15600

Conservative expected results from Dymethyzine within a 2 to 3 week cycle is 15 pounds of solid muscle tissue gains. No additional fat or water retention will accumulate (Dymythyzine does not aromatize). Also, a drastic reduction in previously existing body fat will be noticed. It is so potent and effective a chemical that it is equivalent in growth hormone release to taking 2 IU of Somatropin daily!

Administration: 16 mg per day
Delivery: 22 gauge syringe intramuscularly
Duration: 2-3 week cycle; a minimum 2 week off-cycle
Storage: Refrigerate 36° to 46°
Testing: SMA-25, Chem Profile every two cycles

Catalog

1.0 PRICE LIST FOR SPRING 1985

PRODUCT	STRENGTH	SIZE	PRICE
Adrenalin	1-1000	30 cc	$25.00
Aldactazide		100's	$27.00
Ammonia Ampules		10's	$8.00
Anadrol-50	50 mg	100's	$15.00
Anatrofin	100 mg	1 cc	$9.00
Anavar	2.5 mg	100's	~~$26.00~~ 30.00
Bolasterone (TES-10)	7 mg	30 cc	$255.00
B-complex w/C		20 cc	$25.00
B-12	1000 mg	30 cc	$15.00
Butazolidin	100 mg	100's	$40.00
Chorionic Gonadotropin (HCG)	10,000 Units	10 cc	$26.00
Decadron	0.75 mg	Dose Pak	$25.00
Deca Durabolin (Nandrolone Decanoate)	100 mg	2 cc	$20.00
Delatestryl (Testosterone Enanthate)	200 mg	10 cc	$25.00
Depo (Testosterone Cypionate)	200 mg	10 cc	$23.00
Dianabol	5 mg	100's	$27.00
Dianabol (injectable)	25 mg	10 cc	$28.00
Durabolin-50 (Nandrolone Phenpropionate)	50 mg	2 cc	$22.00
Dyhydrolone (TES-20)	20 mg	30 cc	$280.00
Esciline	4 mg	6 cc	$35.00
Equipoise	50 mg	10 cc	$40.00
Equipoise	50 mg	50 cc	$180.00
Ephedrine Sulphate	3/8 gram	100's	$22.00
Halotestin (Fluoxymesterone)	10 mg	100's	$55.00
Hydergine (sublingual)	0.5 mg	100's	$25.00
Lasix (Furosemide)	40 mg	100's	$27.00
L-Dopa	500 mg	100's	$35.00
Maxibolin	2 mg	100's	$32.00
Methyl Testosterone (oral or sublingual)	10 mg	100's	$24.00
Naprosyn	250 mg	100's	$60.00
Nolvadex	10 mg	60's	$92.00
Parabolan	76 mg	2 cc	$34.00
Potassium (K-Lyte)		30's	$27.00
Primobolan Acetate	20 mg	3 cc	$28.00
Primobolan	50 mg	1 cc	$6.00
Primobolan (buccal tab))	50 mg	30's	$56.00
Primobolan (3 ampule box)	100 mg	3 cc	$46.00
Primobolan S [redacted]	[redacted]	50's	$65.00
Provirn	[redacted]	50's	$45.00
Soma (Carisoprodo [redacted]	[redacted]	100's	$17.00
Sostenon	[redacted]	1 cc	$22.00
STH (Human [redacted]	[redacted]	20 cc	$925.00
Syringes	[redacted]	100's	$25.00
Tetracycline	[redacted]	100's	[illegible]

Testosterone (Aqueous Suspension)	100	mg	10 cc	$21.00
Testosterone Propionate	100	mg	10 cc	$21.00
Thiomucase (cream)			tube	$35.00
Thiomucase (injectable)			10 cc	$60.00
Thiomucase (suppositories)			10 box	$45.00
Thyroid	.2	grams	100's	$24.00
Triacana (cream)			tube	$95.00
Triacana (oral)			100's	$45.00
Trisoralen			28's	$31.00
Winstrol V (Stanozol)	50	mg	10 cc	$50.00
Winstrol V (Stanozol)	2	mg	100's	[redacted] 23.00
Winstrol (brand name)	2	mg	100's	$36.00
Wydase	1500	Units	10 cc	$16.00

Postage -- $6.00
Minimum Order -- $150.00
Cashiers check or money order, Please!
NO PERSONAL CHECKS

2.0 L-DOPA

You may have heard recently of a product currently being used by many strength and physique athletes called Levodopa (Larodopa, L-Dopa). This is an amino acid (available by prescription only) which, when taken orally stimulates the brain to produce dopamine, which is a substance necessary for the body's ability to secrete growth hormone. When a greater amount than usual of this hormone is released, tissue growth (both muscle and tendon) is accelerated and body fat levels drop. Using Levodopa in combination with testosterone and an anabolic agent (such as Deca-Durabolin) can provide a gain of as much as ten pounds of solid muscle in an eight to ten week period. Also, a drop of two to three percent body fat may result. This is a product that is being used instead of the injectable growth hormone, STH, but fortunately, it is available at a fraction of the cost of that product.

Recommended Dosage

Begin your ten week L-Dopa cycle taking two tablets per day (separately at mealtime), gradually increasing the dosage to six to eight tablets taken throughout the day. See package insert. If you feel nauseous, decrease the dosage slightly until your stomach becomes more tolerant. Two ten week cycles per year should produce the desired results. However, it should be noted that these results may not be seen immediatley. It may take several weeks after the first cycle until a substantial gain in muscle mass is apparent. The same is true of STH. Loss of body fat happens right away. Most importantly, however, this tremendous gain is a permanent phenomenon.

Dietary Adjustments

Because of the increase in muscle growth and fat metabolism, high protein and calorie intake is important. Also vitamin C should be taken (4 to 5 grams per day), choline (2 grams per day) and Hydergine (4 tablets per day). Hydergine is also available by prescription only, but may be requested along with L-Dopa. The purpose for adding this to your supplements is to provide protection for the receptors which absorb the L-Dopa. You need not avoid B-6 (as mentioned in the package insert) as this is only a complication if you are being treated for Parkinsonism.

3.0 STEROIDS: FACTS AND APPLICATIONS

Use good judgement in introducing drugs never used before. Use new products alone for one week, then wait 10-14 days to ascertain that your body can tolerate them.

Lifters want an increased strength (androgenic) response as they go through the cycle. Physique athletes want early strength (for size) initially, followed by retention of size, along with the desired definition and vascularity, as the Anabolic effect is increased.

Notice the blending in and out of the different drugs on the peaking routines. Smooth transitions through the spectrum are important. Also, the ratio of one product to another and the principles behind them, are important, not the actual number of pills or cc's, since different products are of varying strengths. Remember, more is not necessarily better. The ratio of the fade in/fade out of the drugs is the crucial part of a successful cycle.

Peakdown is used for smooth transitions back to normal hormone levels.

These products are relatively safe when used intelligently. Many competitors have a blood profile test performed by a physician betweeh cycles. This assures the athlete that it is safe to start his next cycle. A six week time-off period is the minimum recommended between cycles. Many people train year round on drugs. That is a personal decision. The appropriate lay-offs are very important.

Any steroid puts extra stress on the liver. Alcohol is also a liver stressing drug. It is necessary to use alcohol in great moderation, if at all during a steroid cycle.

Injectable products are safer and more efficient than orals. However, the best possible gains are to be made by a balance of both forms of these products.

It should be understood that the cycles supplied at the end of this handout are only guidelines for you to follow. Everyone responds a little differently to every drug.

3.1 ORALS

All steroids have identical properties. They have both anabolic (tissue building) and androgenic (strength) actions. Since clinical separation of these effects has not been accomplished, a description of the practical applications of steroids is best done by their anabolic/androgenic ratios. The following are listed starting with the most anabolic, and then going through the spectrum to the most andrognic.

3.1.1 Maxibolin - The most anabolic on the market. Mainly tissue building and toning. Very mild, little strength gain, no bodyweight gain. Works well for some people.

3.1.2 Anavar - Next in line, some strength gains (slow) and good muscle growth. The best oral of its type. A good base. Gain 2-3 pounds of body weight only.

3.1.3 Primobolan (buccal tab) - This is the best and most powerful of all the Primobolan tablets. It is a soft tablet designed to dissolve under your tongue and consequently more gets into your system than the regular tablets. Dosage is one tablet daily or half a tablet twice a day (morning and night). Women could do one tablet every other day or half daily. (50 mg buccal tab, 30 tabs per bottle)

3.1.4 Primobolan S - This Primobolan Acetate in a oral tablet form. You'll see dosages of two or more tabs daily for men, half that for women. It does not cause an allergic reaction like the injection. Dosages have to be higher than the injectable because the drug is partially destroyed in the gastric tract. Dosages range from one or two tablets every other day to two tablets per day. (25 mg tablets, 50 tablet bottle)

3.1.5 Winstrol - The most balanced oral. Approximately [illegible] anabolic and 50% androgenic. Good strength gains, substantial bodyweight gains.

3.1.6 Dianabol - The best oral for peaking, very androgenic, much weight gain, good for explosive strength. Good to peak on and excellant size builder for bodybuilders.

3.1.7 **Methyl Testosterone Sublingual - Instant response for 2-3 hours. Aggression good for heavy workouts. You can build up a tolerance in 3 weeks, so usage should be discontinued** 7-10 days before a meet where it may be taken at intervals.

3.1.8 Anadrol - Makes you very aggressive and explosive. Used last two weeks by advanced litters; 2-5 per day according to bodyweight.

3.1.9 Halotestin - The most androgenic oral on the market. Do not train on this drug. Use the last 14 days; 1-2 per day. Aggression, explosiveness.

3.2 INJECTABLES

3.2.1 **Primobolan** - The most anabolic. Good for conditioning phase of a lifter and cutting phase of a bodybuilder. Long acting: use 1 cc a week. Gives you a hard finished look.

3.2.2 **Primobolan Acetate** - This is the most popular and effective steroid to use while dieting. It allows you to keep on more muscle while losing fat, than any other steroid. All the Primobolans do this well, but the Acetate is preferred by most, including all the top bodybuilders. Dosage is one ampule, 20 mg every other day. Some people get an allergic reaction to it, get nauseous, and/or have a painful, swollen injection. It is neither androgenic, nor liver toxic. (Metenolone Acetate inj. 20 mg ampule, 3 ampules per box)

3.2.3 **Primobolan Depot** - This is a longer acting version of the Acetate; It lasts for about a week or longer. It is more cost effective than the Acetate, but doesn't seem to have as much kick. Dosage is about 200 mg per week for men, half that for women. No side effects whatsoever for either sex. It really is better and more effective than the Mexican Primobolan (which is only available in the 50 mg ampule strength) even though it is chemically the same. The Germans have much better quality control. Many use Acetate for cutting and Depot for gaining. (Metenolone depot inj. 100 mg ampule, 5 ampules per box)

3.2.4 **Anatrofin** - Very similar to German Depot Primobolan; used for a hard finished look. Take 1 cc/week.

3.2.5 **Deca Durabolin** - Slow acting (2-3 weeks), very anabolic and refined, some weight gain; good to get toned, increases tightness. Some gain in strength.

3.2.6 **Equipoise** - The best injectable of its class. Long acting; use 1-3 cc/week. Tremendous for energy and recovery.

3.2.7 **Durabolin 50** - Fast acting (1 week), very balanced, 50% anabolic 50% androgenic, good weight and strength gains.

3.2.8 **Injectable Winstrol V** - Quick acting, water based, 1 cc 3 times per week. Good weight and strength gains.

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3.2.9 Delatestryl - Slow acting (2-3 weeks), well balanced. approximately same overall effects as Durabolin 50, except long duration. Good to peakdown on after a meet. Not as much fluid retention or acne as Depo.

3.2.10 Parabolan - This is a very powerful non-aromatizing, androgenic steroid from France. It shows solid strength increases in many athelets with out the bloat of something like Anadrol or Testosterone. Dosage for men (not recommended for women) is 2 ampules per week, (Trenbolone inj 76 mg ampule, 2 ampules per box).

3.2.11 Testosterone Propionate - Fast acting (4 days). Very androgenic, weight and strength gain. Can be used to supplement Depo; equal parts of each

3.2.12 Injectable Dianabol - Peaking drug only for lifters. Quick acting, 3 cc/week. Do not take in place of oral Dianabol. Good for bodybuilders during growth phase. They may substitute injectable for oral if desired.

3.2.13 Depo Testosterone - The best injectable for peaking. Much strength and bodyweight gains. Very androgenic.

3.2.14 Aqueous Testosterone - Almost purely androgenic. Two day duration. Good for the last 5 days before meet, to peak. Strictly a powerlifter's product.

3.2.15 Sustenon - A mixture of several androgens. Good for peaking, very androgenic. Take 1 cc/week.

All oil based injectables can be mixed in the same syringe, no more than 3 cc/syringe. Spread injectables out to 2 [illegible] times per week. Do not mix oil and aqueous products in the same syringe.

3.3 NEW INJECTABLES

3.3.1 Bolasterone - This is the original East German government issued formula manufactured for athletic use. It has a four component chemical structure with the following nitrogen retention ratings (NRR) (Methyltestosterone has a NRR of 100/100):

Component 1..............340/15
Component 2.............400/100
Component 3.............150/100
Component 4...........1910/1920

Total NRR.............2800/2135

After ten to fourteen days athlete users have noticed a drastic increase in muscle recuperation. A two to three hour decrease in required daily sleeping patterns has also been reported. Bodyweight seems to stabilize when on a competition diet and muscle growth is matched only by the effects of Somatropin when bulking during the off-season.

An excellant base for Bolasterone is Equipoise, an oil-based veterinarian steroid. Equipoise also has been reported to provide substantial strength increases.

A good combination according to users of both Bolasterone and Equipoise is 1 cc per day and 200 per week, respectively. Outstanding mass gains and quality cuts are inevitable.

Finally, a bit of refreshing information about Bolasterone: it is non-toxic and does not aromatize, hence, no water retention!

Administration: 3.5 to 7 mg per day.
Delivery: 20 gauge syringe intramuscularly.
Duration: 60 day cycle recommended.
Testing: No specific runs, standard liver function.

The following two anabolic steroids are included in the same family of the new advanced generation chemicals originating in East Germany. It is common knowledge in the sports world that the eastern block countries (e.g. the Soviet Union and East Germany) have for many years developed and administered anabolic steroids to their competing athletes. Many Americans feel that this research has given the Eastern block countries an unfair advantage over their peers, especially in strength in muscle oriented sports.

3.3.2 Dyhydrolone - This product is being hailed in the United States as a major breakthrough for use by powerlifters. Its potential strength gains surpass any other anabolic steroid available in the free world today. Through its use a powerlifter should expect to gain at least 20 pounds of bodyweight within two weeks. Accompanying this size will be some water retention, so it is recommended that the powerlifter use one Proviron tablet daily, thereby minimizing this side effect.

The NRR of Dyhydrolone is the highest available of any anabolic steroid designed for powelifters:

Component 1............4000/500
Component 2............2200/300
Component 3...........1000/1000
Component 4..............500/20

Total NRR.............7700/1820

Administration: 20 mg per day.
Delivery: 22 gauge syringe intramuscularly.
Duration: 4-6 week cycle; a minimum 4 week off-cycle.
Storage: Refrigerate 36-46 degrees Fahrenheit.
Testing: SMA-25, Chem. Profile every cycle.

3.3.3 Dymethyzine - This product is the most outstanding anabolic steroid ever benefited by bodybuilders. It is the only chemical so high in NRR that it actually alters the RNA/DNA predetermined muscle fiber [illegible] (a hyperplasia inducing agent):

Component 1...........4000/2000
Component 2...........[illegible]300/6500
Component 3...........10000/7500
Component 4...........1200/100

Total NRR.............17500/15600

Conservative expected results from Dymethyzine within a two to three week cycle are 15 pounds of solid muscle tissue gains. No additional fat or water retention will accumulate (Dymethyzine does not aromatize). Also, a drastic reduction in previously existing body fat will be noticed. It is so potent and effective a chemical that is equivalent in growth hormone release to taking two IU of Somatropin daily.

Administration: 16 mg per day.
Delivery: 22 gauge intramuscularly.
Duration: 2-3 week cycle; minimum 2 week off-cycle.
Storage: Refrigerate 36-46 degrees Fahrenheit.
Testing: SMA-25, Chem Profile every two cycles.

4.0 MISCELLANEOUS PRODUCTS

4.1 STIMULATORS

4.1.1 Adrenalin - The real thing. Very potent and short lived. Use 1/2 to 1 cc only and only for the deadlift. I.M. only; aspirate syringe before injection. Use 20 minutes before the deadlift.

4.1.2 Ephedrine Sulphate - Antihistimine that has a stimulant effect. Good for training or contest.

4.1.3 Thyroid - Metabolic stimulant, burns subcutaneous body fat first.

4.1.4 Human Chorionic Gonadotropin (HCG) - For people with weight problems, use for the last 4-5 weeks: 1 to 3 times a week, 10,000 units, bodybuilders use same dosage for cutting and vascularity. Continued use after a contest helps body return to normal hormone levels. Dosage for HCG after discontinuation of steroids, in order to bring the body back to normal hormone levels, should be 1-2 cc's every other day for 2-3 weeks.

4.2 ANTI-INFLAMATORY PRODUCTS

4.2.1 Naprosyn - The best for training. As with all anti-inflamatory products, they only help bones, joints, and tendons. It is an aspirin derivative; very safe; take one, 3-4 times per day after meals.

4.2.2 Decadron - For acute pain during heavy training only. Follow dosage on package exactly.

4.2.3 Butazolidin - Very good for inflamed muscles and minor injuries. Speeds up the healing process. Take one, 3-4 times per day after meals. Don't use for more than five days.

4.3 DIURETICS

4.3.1 Aldactazide - The best for making weight without strength loss. Slow acting (10 hours) and not very potent. Potassium sparing, means less cramping. Take 1-2 tablets per day.

4.3.2 Lasix - Very potent; weight and strength loss plus possible cramping. Use only in emergencies. Quick acting (4 hours), 1-2 tablets.

4.4 OTHER

4.4.1 Soma - Musqle relaxant that works on skeletal muscle. Good for pulled muscles, strains, and cramps, because it allows the muscle to relax during sleep while they are being repaired. Also good for troubled sleep. Take 1-2 tablets at bedtime.

4.4.2 Potassium - For making weight; cramps; add calcium and magnesium, also.

4.4.3 Tetracycline - Best broad spectrum antibiotic for steroid related acne. Is not protein catabblic, so does not effect training. Take one, 2 times per day for 1 week, then 1 at bedtime thereafter. These instructions are for the 500 mg tablets, if you have the 250 tablets, then double the number of tablets taken in the above instructions. Avoid taking an hour before or after dairy products or antacids.

4.4.4 Wydase - A drug dispersant. Injectable only, it is mixed with HCG or STH (equal parts). Used alone it does nothing, but in conjunction with the above, it allows the products to be absorbed more readily.

4.4.5 Nolvadex - An estrogen prohibitor. Decreases your body's estrogen to minimize feminine characteristics. Non-steroidal. Take 1-4 per day.

4.4.6 Provirn - [illegible] estrogen production, [illegible] characteristics. Also has some [illegible] retention. Take 1-2 tablets [illegible] the evening.

4.4.7 Somatropin (STH) - Totally unlike steroids in action and effect. Not for peaking, it is a slow, steady foundation builder of permanent muscle tissue. Promotes fat loss, muscle gain concurrently. Quick acting, 1 cc 3 times/week. Always rotate injection site; Deep I.M. Diet is equally as important as training; greatly increase calories and vitamins for 12-14 weeks. Always take STH in conjunction with steroids; synergistic. Usually takes several weeks to get total results. 70% of your full potential will be reached in the first cycle.

4.4.8 Trisorolan - Sun tan pills. Potentiate the sun's tanning power. Tan twice as fast. Follow directions on package insert for dosage.

4.4.9 Levo-dopa (L-Dopa) - An amino acid which stimulates the brain to produce dopamine, a substance necessary for the body to produce growth hormone. Using L-Dopa in combination with Testosterone and an anabolic agent like Deca-Durabolin, can provide exciting permanent gains. Requires a high calorie, high protein diet; extra vitamin C, and Hydergine tablets (2/day). The Hydergine serves to protect the growth hormone receptors and should be requested with the L-Dopa. Begin your 10 week L-Dopa cycle taking 2 tablets per day, gradually increasing the dosage to 6-8 tablets taken throughout the day. Not a steroid; stimulates the natural growth hormone present in both men and women.

4.4.10 B-12 and B-Complex - The B vitamins (which are so important) in injectable form. Good for energy, recovery and increasing appetite. Take 1 cc, 3 times per week.

4.4.11 Esiclene - This Italian Steroid was very popular in the mid seventies, but had become unavailable for a few years. Esiclene has the reputation of:

1) making you look very defined and vascular.

2) making the specific muscle area that you inject it into grow!

The injection of [illegible] Esiclene is also accompanied with 20 mg [illegible] killer), so Esiclene will indeed [illegible] areas swell because the steroid will cause [illegible] irritation and lymph in the area. Knowing this [illegible] Esiclene can be used the last two weeks before [illegible] to enlarge weak areas such as calves, biceps, rear delts, etc. Everyone who has used

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this drug swears that it works! It is water based and should be injected with an insulin or vitamin needle (i.e. 25 or 26 gauge, one-half inch). Dosage can only fix two body parts at once. Some very noteworthy national caliber physiques use Esiclene for contest prep. (Formebolone inj. 4 mg ampules, 6 ampules per box).

4.4.12 Thiomucase - This is an injectable which is freeze dried (you reconstitue it before the injection with the solvent supplied). Thiomucase is a spreading agent enzyme that was originally developed to diffuse the injection from the injection site, so drugs would take effect quicker than usual. It also allows water to escape from fat cells. Fat usually holds about 15% of its weight in water, but excess estrogen, such as some steroids turn into, can make fat cells hold more. Women usualy have more water than mem in their fat cells. You can use Thiomucase injection in three ways:

1) you can mix it with any injectable steroid, even oil based drugs so that they will get into your system quickly.

2) you can inject it with an insulin needle in tiny amounts into fatty areas you want to reduce.

3) you can mix the freeze dried powder with a small amount of DMSO to the consistency of a very thin and runny paste, then rub this mixture onto the problem fat areas.

The fat injection method is slightly painfull. Thiomucase and DMSO is very effective (DMSO is an excellant solvent). You should be using about two ampules a day for about a week to ten days before the contest. (inj. 10 ampules per box)

4.4.13 Thiomucase Cream - This is a tube of Thiomucase dissolved in Formaldehyde, which is a good, safe, fairly oderless solvent that has the effect of dropping the Thiomucase through the skin and into the fat cells. DMSO would be a better solvent, but that home brew is inconvenient, messy, and, well, some people don't like the taste of DMSO. Apply the cream twice a day to the problem areas (unless your entire [illegible] problem area). A tube should last you anywhere between three days to one week. You should use [illegible] 10 days before a contest.

4.4.14 Thiomucase Suppositories - This is the easiest way to take Thiomucase and for some reason is pretty effective. Most people take two per day, one before bed and one in the morning, for about five days before a contest. This is used along with the cream and the injection. (10 per box)

4.4.15 Triacana - This is a very safe and popular thyriod type drug. It is not exactly a thyroid and is supposed to work mostly and directly on fat metabolism without disturbing muscle mass, body temperature, heart rate, etc. Triacana is very popular with European bodybuilders. There are many wonder stories about hardening up with its use. It can be used up to two months before a contest, but most use it the last three weeks. Dosage is at least four a day, with an average of 6-12 tabs per day (for men). It acts somewhat like Cytomel, but does not have the bad side effects. (100 tabs per box)

4.4.16 Tricana Cream - This should be used in addition to the tablets. It is applied to the problem areas (fat), and will sink through the skin, acting directly on the fat cells. This is a very clever product, and may be the solution (along with Thiomucase) to spot reduction, especially for women bodybuilders.

Catalog

STRENGTH AND SIZE

Anabolic Steroids:

These are synthetic derivatives of testosterone, and are used primarily for their protein-anabolic as well as catabolic-inhibiting effects upon tissue. They work best when caloric and protein intake is sufficient. By improving the nitrogen balance, they speed up and "enhance" the muscle-building effects of weight-training exercises, but are also useful adjuncts during periods of extreme caloric and/or protein dietary restriction, serving to maintain existing muscle mass.

The desirable "anabolic" effects have not been completely dissociated from several undesirable "androgenic" effects, which may include any of the following: 1) elevated serum cholesterol levels 2) inhibition of testicular function 3) oligospermia 4) gynecomastia 5) changes in libido 6) gonadotropic inhibition 7) edema 8) cardio-vascular disease 9) hypertension 10) renal difficulties 11) hirsutism 12) acne 13) male pattern baldness.

In addition, the presence of an alpha alkyl group at the C-17 carbon of many steroids can cause other problems, namely: 1) hepatocellular neoplasms 2) peliosis hepatis 3) cholestasis 4) jaundice.

Generic Label: methandrostenolone.

Trade Label: 1. Dianabol (discontinued)

How Supplied: 2.5 and 5 mg tablets, bottles of 100 and 500

25 mg/ml injectable, 10 cc vials

Clinical Dosage: 5 mg daily

* **1984 List Price:** $8.00 @ 100 (5 mg generic)

Comments: Easily the most popular oral steroid; good for bulking and strength-building; fairly [illegible] long-lasting.

* WHOLESALE PRICES ONLY; DEALER MARKUPS NOT INCLUDED

STRENGTH AND SIZE

Generic Label: oxandrolone

Trade Label: 1. Anavar

How Supplied: 2.5 mg tablets, bottles of 100

Clinical Dosage: 10 - 20 mg daily

1984 List Price: $17.00 @ 100

Comments: Does not aromatize, very safe oral; low androgenicity, good for maintaining muscle mass while dieting; fast-acting.

Generic Label: oxymethelone

Trade Label: 1. Anadrol
2. Adroyd

How Supplied: 50 mg tablets, bottles of 100 (Anadrol)
2.5, 5, and 10 mg tablets, bottles of 100 (Adroyd)

Clinical Dosage: 5 - 15 mg daily (Adroyd)
1 - 5 mg/kg bodywt. daily (Anadrol)

1984 List Price: $55.00 @ 100 (Anadrol - dealer)

Comments: Perhaps the crudest of all orals, with highest incidence of clinical hepatic damage; still very popular for strength and bulking effects; very rapid action, used for peaking in combative sports during last 4 - 6 weeks.

Generic Label: stanozolol

Trade Label: 1. Winstrol [illegible]
2. Stromba
3. Winstrol [illegible]

How Supplied: 2 mg tablets, [illegible] (Winstrol) [illegible]

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STRENGTH AND SIZE

25 mg/ml injectable, 10 cc vials (Stromba)

Clinical Dosage: 6 mg daily (Winstrol)

2 cc/wk (Stromba)

1984 List Price: $11.00 @ 100

$30.00 @ 10 cc (Stromba - dealer)

Comments: Mildly androgenic, fairly anabolic oral; used by some to retain muscle mass while dieting; does not aromatize, very fast-acting.

Generic Label: ethylestrenol

Trade Label: 1. Maxibolin
2. Orabolin
3. Ourabolin

How Supplied: 2 mg tablets, bottles of 100

Clinical Dosage: 4 - 8 mg daily

1984 List Price: $13.00 @ 100

Comments: C-17 carbon not alkylated, hence safest oral steroid for liver; very low androgenicity, used primarily for cutting excess water by bodybuilders; very fast-acting.

Generic Label: methandriol dipropionate

Trade Label: 1. Therabolin

How Supplied: 50 mg/ml injectable, 10 cc vials

Clinical Dosage: 2 cc/wk.

1984 List Price: $11.00 @ 10 cc (dealer)

STRENGTH AND SIZE

Comments: Popular injectable used for cutting-up and maintaining muscle mass while dieting; very low androgenicity, very fast-acting.

Generic Label: nandrolone decanoate

Trade Label: 1. Deca-durabolin
2. Nandrolate

How Supplied: 50 and 100 mg/ml injectable, 2 cc vials

200 mg/ml injectable, 1 cc vials

Clinical Dosage: 100 mg every 3 - 4 weeks

1984 List Price: $3.40 @ 2 cc (100 mg/ml generic)

Comments: Long-lasting, highly refined steroid; good for strength-building as well as peaking cycles for bodybuilding; very low androgenicity makes this drug popular among the safety-minded.

Generic Label: nandrolone phenylpropionate

Trade Label: 1. Durabolin
2. Neutrosteron

How Supplied: 25 mg/ml injectable, 1 or 5 cc vials

50 mg/ml injectable, 2 cc vials

Clinical Dosage: 25 - 50 mg/wk

1984 List Price: $1.60 @ 2 cc (50 mg/ml generic)

Comments: Another good injectable; long-lasting, much the same effect as Deca-durabolin or Methandriol.

4

Generic Label: methenolone

Trade Label: 1. Primobolan

How Supplied: 50 mg/ml injectable, 1 cc vials

Clinical Dosage: 50 mg/wk

1984 List Price: $5.00 @ 1 cc (dealer)

Comments: Popular drug from Germany; very fast-acting; similar in action to Deca-durabolin.

Generic Label: methenolone acetate

Trade Label: 1. Primobolan Acetate

How Supplied: n/a

Clinical Dosage: n/a

1984 List Price: n/a

Comments: Number one injectable used for peaking phases of bodybuilding; lowest androgenicity of most steroids; obtained in Europe or Mexico.

Generic Label: dromastanolone propionate

Trade Label: 1. Drolban

How Supplied: 50 mg/ml injectable, 10 cc vials

Clinical Dosage: 100 mg 3 times/wk

1984 List Price: n/a

Comments: Somewhat androgenic, but superior in most aspects to the best testosterone injectable; good for bulking and strength-building.

STRENGTH AND SIZE

Androgens:

The androgens are also derivatives of endogenous testosterone, and like the anabolic steroids, also exhibit protein-anabolic as well as catabolic-inhibiting effects. Unlike anabolic steroids, however, the androgens are considerably more androgenic, having been synthesized primarily for the purpose of clinical hormone-replacement therapy. While offering perhaps a more cost-effective means with which to enhance muscle growth, androgens are less desirable due to their extreme androgenicity. Associated side-effects are similar to those of anabolic steroids.

Generic Label: testosterone cypionate

Trade Label: 1. Depo-testosterone
2. Vigorex

How Supplied: 50, 100, and 200 mg/ml injectable, 10 cc vials

Clinical Dosage: 1 - 2 cc every 2 weeks (200 mg/ml)

1984 List Price: $5.00 @ 10 cc (200 mg/ml generic)

Comments: Popular, but very androgenic injectable; least desirable of testosterones from androgenic standpoint; good for bulking and strength-building.

Generic Label: testosterone enanthate

Trade Label: 1. Delatestryl
2. Andropository

How Supplied: 200 mg/ml injectable, 10 cc vials

Clinical Dosage: 2 cc/month

1984 List Price: $5.00 @ 10 cc (generic)

Comments: Less androgenic than [illegible] faster-acting. [illegible]

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STRENGTH AND SIZE

Generic Label: testosterone propionate

Trade Label: 1. Perandren

How Supplied: 50 and 100 mg/ml injectable, 10 cc vials

5 mg sublingual tablets, bottles of 100

Clinical Dosage: 50 mg twice/wk (injectable)

1984 List Price: $10.00 @ 10 cc (100 mg/ml - dealer)

Comments: Best testosterone preparation; relatively low androgenicity; very fast-acting; good strength and bulking drug.

Generic Label: testosterone, aqueous

Trade Label: n/a

How Supplied: 25, 50, and 100 mg/ml injectable, 10 cc vials

1984 List Price: $3.20 @ 10 cc (100 mg/ml generic)

Comments: Fastest-acting testosterone; very difficult to maintain constant serum levels; extremely potent androgen, used by many just prior to contest to enhance aggression; must be administered every 48 hours under close supervision.

Generic Label: methyl-testosterone

Trade Label: 1. Metandren
2. Neo-Hombreol M
3. Oreton Methyl
4. Vigorex Capsules
5. Android
6. Virilon
7. Testred

How Supplied: 10 mg tablets, bottles of 100 (oral/ sublingual)

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Clinical Dosage: 10 - 40 mg daily

1984 List Price: $1.85 @ 100 oral/sublingual (generic)

Comments: Oral tabs are twice as potent as sublinguals; similar in action to testosterone propionate, but much more androgenic; jaundice may result with severe abuse.

Generic Label: fluoxymesterone

Trade Label: 1. Halotestin
2. Android F
3. Ora-testryl
4. Vitandren

How Supplied: 2.5, 5, and 10 mg tablets, bottles of 100

Clinical Dosage: 10 mg daily

1984 List Price: $56.00 @ 100 (10 mg tablets)

Comments: Considerably more potent than methyl-testosterone; fairly anabolic, with same androgenicity as most testosterones; very toxic to liver.

Generic Label: boldenone undecylenate

Trade Label: 1. Equipoise

How Supplied: 50 mg/ml injectable, 10 cc vials

Clinical Dosage: n/a

1984 List Price: $15.00 @ 10 cc

Comments: Veterinary drug; similar in activity to testosterone cypionate.

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Gonadotropic Hormones:

Gonadotropins are polypeptide hormones which can elicit secondary hormonal release within the gonads or sex-organs of humans. Accordingly, chorionic gonadotropin, which is produced in the placenta, can stimulate the testes to produce testosterone in males. This is mainly due to the structural similarities between chorionic gonadotropin and luteinizing hormone.

Athletes using this drug ofen take it in combination with anabolic steroids and androgens in order to combat dysfunction of the gonads. However, use of chorionic gonadotropin will shut down the natural luteinizing hormone output in ones body. Additional side-effects may include 1) edema 2) vascular inflammation 3) elevated levels of estradiol and progesterone in male users.

Generic Label: chorionic gonadotropin

Trade Label: 1. A.P.L.
2. Profasi H.P.

How Supplied: 5000, 10000, and 20000 units dry chorionic gonadotropic powder plus 10 ml sterile diluent ampul

Clinical Dosage: 500 - 1000 units 3 times/wk for 3 weeks, then 2 times/wk for 3 weeks

1984 List Price: $8.00 @ 10000 units

Comments: Popularly used when coming off regular drug cycles in order to promote "rebound" effect with plasma testosterone levels; will not counteract oligospermia; used by some to up "natural" testosterone levels without concomitant use of other drugs, especially prior to drug-tested competition.

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STRENGTH AND SIZE

Somatotropic Hormones:

These hormones are pituitary in origin and influence the rates of growth. Use of these substances by athletes often results in thickened cartilage and bone development of the joints, due to production of a substance called somatomedin. In addition, somatomedin is responsible for collagen formation in the skin, and results in a coarsened, thickened texture to the epidermis. The more desirable effects of somatotropic hormones are increased protein-synthesis, as well as increased fatty acid mobilization for energy usage. However, this fatty acid release into the bloodstream can overload the pancreas with excessive amounts of unused glucose and indirectly cause hyperinsulinism. Moreover, this condition can eventually lead to a diabetagenic state.

Although some controversy still exists as to the true efficacy of somatotropic hormones for ergogenic purposes (since it is rarely used without concomitant steroid ergogens), this substance is gaining widespread popularity. Short supply of this pituitary hormone (which is taken from human cadavers) makes it quite expensive, and raises a unique moral dilemma as to whether the questionable ergogenic needs of otherwise healthy athletes should take precedence over the intended clinical applications for patients deficient in this rare substance.

Generic Label: somatropin

Trade Label: 1. Asellacrin
2. Crescorman

How Supplied: 2 and 10 unit vials, to be reconstituted with 5 ml bacteriostatic water vial (Asellacrin)

4 unit/vial with 2 ml NaCl ampul (Crescorman)

Clinical Dosage: 1 unit 3 - 4 times/wk

1984 List Price: $60.00 @ 4 units (Crescorman - dealer)

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Comments: Highly anabolic; gains rapid, but not permanent; prohibitive cost still makes this a questionable value when compared to other steroids, although STH may be a safer alternative (7).

Anti-Parkinsonians:

Anti-Parkinsonians are drugs which are used to combat Parkinson's disease, a disorder involving the catecholamine neurotransmitters. The anti-Parkinsonians listed in this guidebook include the following: 1) Larodopa, 2) Sinemet, 3) Carbidopa-Levodopa, 4) Levodopa, 5) Parlodel.

These synthetic preparations all possess dopaminergic properties, meaning that they help elevate the body's natural supply of dopamine, an important neuro-transmitter. The anti-Parkinsonians also are believed to indirectly stimulate release of the natural pituitary growth hormone, and it is for this reason that many athletes subscribe to their use.

Some of the more common side-effects associated with the usage of dopaminergic stimulants include nausea and disruption of CNS activity. Dosage modification may alleviate these problems, as may individual drug tolerance over a peiod of time.

Generic Label: propanoic acid monohydrate

Trade Label: 1. Sinemet
2. Carbidopa-Levodopa

How Supplied: tablets with 1:4 ratio of carbidopa to levodopa (25 mg / 100 mg)

tablets with 1:10 ratio (25 mg / 250 mg and 10 mg / 100 mg)

Clinical Dosage: 1 tablet (1:4) 3 times/day initially, then increased every other day until maximum of 8 tablets is obtained.

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STRENGTH AND SIZE

1984 List Price: $20.00 @ 100 (10/100 Sinemet)

Comments: Not to be taken concurrently with Larodopa (see); B6 does not affect Sinemet due to presence of carbidopa; less incidence of nausea and malaise with this drug, although still high incidence of CNS (central nervous system) disturbances; popularly used with concomitant steroid ergogens.

Generic Label: dihydroxyphenyl alanine

Trade Label: 1. Larodopa
2. Levodopa (L-Dopa)

How Supplied: 100 mg, 250 mg, or 500 mg tablets of 100 or 500 per bottle

Clinical Dosage: 500 - 1000 mg daily up to 8000 mg daily

1984 List Price: $20.00 @ 100 (500 mg dealer)

Comments: B6 in doses of 10 - 25 mg daily will neutralize action; anorexia, fatigue, malaise, and CNS disturbances common with this drug; actions similar to Sinemet.

Generic Label: bromocriptine mesylate

Trade Label: 1. Parlodel

How Supplied: 2.5, 5 mg tablets of 30 or 100 per bottle

Clinical Dosage: 5 mg daily, increased by 2.5 mg every 28 days

1984 List Price: $33.50 @ 30 tablets (5 mg)

Comments: Often used adjunctively with L-Dopa as treatment for Parkinson's Disease; adverse reactions same as L-Dopa or worse.

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Anti-Diuretics:

These drugs are clinically employed to reduce polydipsia, polyuria, and dehydration. Lypressin, the only anti-diuretic listed in this guidebook, is a synthetic polypeptide hormone preparation that also bears similar actions to that of arginine-8-vasopressin, the anti-diuretic hormone of the posterior pituitary gland. Ergogenic effects include growth-hormone release as well as increased coordination and concentration. Undesirable effects may include occasional headaches, intestinal cramping, and angina pectoris for susceptible individuals.

Generic Label: lypressin

Trade Label: 1. Diapid

How Supplied: 50 posterior pituitary units in 8 ml spray bottle

Clinical Dosage: 1 spray (2 units) 4 times daily in each nostril

1984 List Price: n/a

Comments: Action lasts 3 - 6 hours.

Anti-Histamines:

Histamines are substances which are often released by ones body in response to certain stressors (e.g. allergens), and can have certain negative effects upon body tissues in excessive amounts (e.g. rhinitus, or runny nose, etc.). Accordingly, anti-histamines are those drugs which help to block the effects of excessive histamine release and which also help to indirectly alleviate some of the complications as well.

One anti-histamine in particular, Periactin, is [illegible] by some to possess certain ergogenic properties.

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Experiments have shown that Periactin can stimulate ones appetite, and may even possibly enhance muscle growth. Unfortuhately, one of the side-effects of this drug include extreme drowsiness in high dosages. Use of this substance remains limited.

Generic Label: cyproheptadine hydrochloride

Trade Label: 1. Periactin

How Supplied: 4 mg tablets, bottles of 100

Clinical Dosage: 4 - 20 mg daily

1984 List Price: $2.40 @ 100 (generic)

Comments: Very popular during the 1960's before steroid use became very widespread.

Anti-Neoplastics:

These drugs are used to combat cancer, particularly carcinoma of the breast. They exhibit anti-estrogenic effects due to their ability to compete for binding sites in target tissue (breast), and it is this special property which is of particular interest to lifters. Owing to the body's tendency to aromatize certain steroid and androgen preparations, testosterone is converted to estrogen. This aromatization of testosterone leads to several unwanted side-effects, one of which is gynecomastia, or the development of breast-like tissue. Also, a rapid drop in testosterone levels following aromatization precedes a considerable loss of strength and size.

For those athletes who wish to minimize these side-effects, the concomitant use of an anti-neoplastic bearing anti-estrogenic properties is usually advised by many drug "experts". While there are no known contra-indications to use of these drugs, their use may elicit the following effects: 1) vomiting [illegible] nausea.

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Generic Label: tamoxifen citrate

Trade Label: 1. Nolvadex

How Supplied: 10 mg tablets, bottles of 60 and 250

Clinical Dosage: 20 - 40 mg daily

1984 List Price: $46.00 @ 60

Comments: Will not remove gynecomastia; only complete drug abstention or medical intervention will help serious cases.

Generic Label: testolactone

Trade Label: 1. Teslac

How Supplied: 50 or 250 mg tablets, bottles of 100

Clinical Dosage: 250 mg daily

1984 List Price: n/a

Comments: Similar in action to Nolvadex.

Lipotropics:

These are drugs commonly used by physicians to lower serum cholesterol, triglyceride, and lipid concentrations. Nicotinic acid (niacin) is the only lipotropic listed in this guidebook due to its ready availability and widespread use among bodybuilders.

Nicotinic acid in large enough quantities has powerful pharmacologic effects, otherwise it is more commonly employed as a B vitamin. Bodybuilders tend to use this drug simply for its "flushing" effects, due to peripheral vasodilation within the skin tissue. The flushing is believed by many to enhance the tanned appearance of a physique while onstage. Heavy abuse of this substance can cause hepatic and gastro-intestinal problems, as well as skin-irritation. Use should be

STRENGTH AND SIZE

[redacted]

monitored if prolonged. [redacted]

Generic Label: nicotinic acid

Trade Label: 1. Nicolar

How Supplied: 500 mg tablets of 100 per bottle

Clinical Dosage: 1 - 2 grams daily

1984 List Price: $5.00 @ 100 (generic)

Comments: Substitute niacinimide for nicotinamide for a less pronounced flushing effect and less itching, or use with meals; tolerance to itching may develop with time.

Spreading Agents:

Hyaluronidase, the only spreading agent covered in this guidebook, is a preparation of bovine testicular hyaluronidase, a potent enzyme. This substance acts to hydrolyze hyaluronic acid, a viscous polysaccharide found in interstitial tissue. This effect serves to permit easier and more rapid diffusion of fluids in tissue, hence the "spreading" quality.

Specifically, there is a belief among certain circles that spreading agents help mobilize fat and can enhance the "defining" process of pre-contest training. This is completely unfounded, and ignores the true clinical applications of this special category of drugs.

A more realistic assessment of spreading agent use in athletics involves the concomitant administration of minute quantities of hyaluronidase with other injectables to facilitate more rapid absorption. Still, this drug continues to be used mistakenly by bodybuilders as a "fat mobilizer", along with another European ergogen, Thiomucase. [redacted]

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Generic Label: hyaluronidase

Trade Label: 1. Wydase

How Supplied: 1500 units, vials of 10 cc

Clinical Dosage: administered concomitantly with other drugs to facilitate absorption (150 units for 1000 cc or more).

1984 List Price: $5.20 @ 10 cc

Comments: Used with epinephrine injections to eliminate "lag time"; well-tolerated; do not administer into inflamed areas.

Thyroid:

Thyroid hormones promote generalized increases in body metabolism, and are popular with some athletes because of their supposed "calorie-burning" effects, particularly bodybuilders dieting for a contest. Unfortunately, use of thyroid in otherwise healthy individuals will do more than burn calories. Side-effects may include 1) loss of muscle tissue 2) cardiac arrythmias 3) insomnia 4) tachycardia 5) nausea 6) diarrhea 7) fever 8) elevated blood pressure 9) tremors 10) nervousness.

Effects are highly cumulative, sometimes lasting for months following cessation of drug use. Full effects of thyroid preparations usually take from 10 to 14 days.

Generic Label: thyroxine, liothyronine

Trade Label: 1. Thyroid
2. Thyroid Strong
3. Synthroid
4. Thyrolar
5. Euthroid
6. Cytomel
[illegible]

[illegible] and 2 grain tablets of 100 or 1000 (Thyroid Strong)

STRENGTH AND SIZE

Clinical Dosage: 1/2 to 2 grains daily; varies considerably

1984 List Price: $15.45 @ 2 grain (Thyroid Strong - 1000)

Comments: Popular with many bodybuilders, but loss of strength and size due to muscle catabolism is inevitable.

Food Coloring Additives:

- Canthaxanthin, an FDA-approved red food coloring agent, is not without certain ergogenic applications for those seeking a tan without exposure to the sun.

Chemically a carotenoid like beta carotene, canthaxanthin has been found to be generally harmless and capable of eliciting a bronze skin tone in users. Not only is no ultra-violet radiation required, but this "pseudo-tan" also provides protection against UV damage.

However, canthaxanthin use is not without hazards: acute overdosage can cause gastro-intestinal upset, and chronic overdosage can cause a bright red to orange tint in the skin that may take weeks to dissipate.

Generic Label: canthaxanthin

Trade Label: 1. Easy Tan
2. Orobronze

How Supplied: 30 mg tablets, bottles of 80 (Easy Tan)

Manufacturer's Recommended Dosage: 120 mg daily

1984 List Price: $30.00 @ 80 tablets (Easy Tan)

Comments: This substance occurs naturally in mushrooms, shellfish, and [illegible] gaining in popularity where [illegible] is hard to come by. [illegible]

CNS Stimulants:

These drugs consist of the amphetamines and related compounds, epinephrine (adrenalin), and caffeine-containing compounds. All in some way effect either the central nervous system and/or the sympathetic nervous system.

Their primary actions are to stimulate the nervous system, and also to act as respiratory, circulatory, and psychomotor stimulants. Clinically, many of these drugs are used as treatment for such varied conditions as CNS depression, circulatory failure, respiratory depression, narcolepsy, hyperkinesia, exogenous obesity (as appetite suppressants), minimal brain dysfunction, or to treat mucosal congestion.

Side-effects from overdosage might include any of the following: 1) vertigo 2) nervousness 3) insomnia 4) anorexia 5) headache 6) dyskinesia 7) tachycardia 8) angina 9) cardiac arrythmias 10) abdominal pains 11) sweating 12) blood pressure changes 13) vomiting 14) dryness in mouth 15) false euphoria 16) nausea 17) drug-dependency.

Ergogenic use of CNS stimulants among athletes stems from the belief that these compounds temporarily enhance both aerobic and anaerobic power. Unfortunately, the accompanying lack of coordination, dizziness, and false euphoria (making the athlete oblivious to pain and injury) which usually results from stimulant abuse can make these drugs a questionable ergogenic choice for combative events. Nevertheless, they remain quite popular as both competitive and training aids for many strength athletes.

Generic Label: methylphenidate

Trade Label: 1. Ritalen

How Supplied: 5, 10, and 20 mg tablets, bottles of 100

[illegible] 20 - 30 mg daily.

[illegible] 15.00 @ 100 (5 mg)

[illegible] commonly used to treat hyperactivity in children; a rather mild stimulant.

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PERFORMANCE

Generic Label: dextroamphetamine sulphate

Trade Label: 1. Dexedrine
2. Benzedrine

How Supplied: 5 mg tablets, bottles of 100 and 500

5, 10, and 15 mg capsules, bottles of 50

Clinical Dosage: lowest effective dosage

1984 List Price: $56.00 @ 500 (10 mg tablets — Dexedrine)

$30.00 @ 500 (10 mg tablets — Generic)

Comments: Commonly used as dietary-aids in clinical contexts; high risk of dependency associated.

Generic Label: nikethamide

Trade Label: 1. Coramine
2. Nikorin

How Supplied: 25% aqueous injectable, 1.5 ml vials

Clinical Dosage: lowest effective dosage

1984 List Price: n/a

Comments: Intravenous or intramuscular administration; potent stimulant actions.

Generic Label: doxapram hydrochloride

Trade Label: 1. Dopram

How Supplied: 20 mg/ml injectable, 20 ml vials

Clinical Dosage: lowest effective [illegible]

1984 List Price: n/a

Comments: Becomes effecti[illegible] stimulant only after [illegible] sufficiently [illegible]

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[illegible] increased.
[illegible]

Generic Label: epinephrine

Trade Label: 1. Adrenalin Chloride
2. Epinephrine
3. Sus-Phrine

How Supplied: 1 mg/ml injectable, 30 ml vials (Adrenalin Chloride)

Clinical Dosage: .2 - 1 mg per injection

1984 List Price: $3.15 @ 30 ml (Adrenalin Chloride)

Comments: Discoloration indicates loss of potency; popular in combative events for short peak-level efforts.

Generic Label: caffeine

Trade Label: 1. No Doz
2. Vivarin

How Supplied: 100 mg tablets, boxes of 15 and 36 (No Doz)

Recommended Dosage: One 100 mg tablet contains approximately same amount of caffeine as found in one cup of coffee

1984 List Price: Prices vary where sold

Comments: A popular over-the-counter product, commonly used as an anti-fatigue stimulant; caffeine is the drug of choice for those wishing good CNS stimulation without many harmful side-effects.

Diuretics

[illegible] covers only 2 common diuretics.

PERFORMANCE

Aldactazide and Lasix. Aldactazide is a combination of 2 diuretic agents, providing additive diuretic and antihypertensive effects. Lasix is an anthranilic acid derivative, and inhibits sodium and chloride reabsorption by the kidneys. Both drugs promote diuresis, or the excretion of sodium and water. Moreover, they are clinically used as treatment for edema and/or hypertension.

Ergogenically, diuretics are used just prior to competition by both bodybuilders and combative athletes to promote the loss of excess water and/or bodyweight. The sometimes high dosages employed under these circumstances often lead to GI cramping and diarrhea in users, due to electrolyte imbalances.

Generic Label: spironazide

Trade Label: 1. Aldactazide

How Supplied: bottles of 100, 500, and 1000

Clinical Dosage: lowest effective dosage

1984 List Price: $4.40 @ 100 (generic)

Comments: Frequent overuse may cause gynecomastia: no potassium supplementation should be used with Aldactazide.

Generic Label: furosemide

Trade Label: 1. Lasix

How Supplied: 20 and 40 mg tablets, bottles of 100 and 500

Clinical Dosage: initial dose of 20 - 80 mg, then a second dose of equal or increased amount no sooner than 6 - 8 hours later [illegible]

1984 List Price: $8.75 @ 100 [illegible]
$12.35 [illegible]

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Comments: The onset of diuresis following administration [illegible] is within one hour; duration of effects is 6 - 8 hours; potassium supplementation is usually required with heavy use of Lasix.

Anti-Diuretics:

These drugs are often used for their ergogenic effects upon coordination and concentrating ability. See "Strength And Size" section, pg. 21.

Geriatrics:

This class of drugs is intended for treatment of conditions found in the elderly. Hydergine, the only geriatric chemical listed in this section, is specifically used by geriatric physicians for ailments of the noradrenergic and dopaminergic nervous systems.

While its ergogenic use remains limited, Hydergine seems capable of maintaining brain energy levels during periods of great stress, which means that better judgement and superior muscular control will result while training or competing.

Its actions are similar to that of another drug, Diapid (an anti-diuretic), insofar as ergogenic applications are concerned.

Generic Label: hydro-ergoloid

Trade Label: 1. Hydergine

How Supplied: 1 mg oral/sublingual tablets, packages of 100 and 500

[illegible] Dosage: 1mg 3 times daily

[illegible] Price: $5.00 @ 100 (sublingual - generic)

Comments: The [illegible] with Hydergine can cause potentiation of caffeine's effects, leading to insomnia and other undesirable side-effects.

Anti-Inflammatories:

This class of drugs is used to combat inflammation, a condition involving histamine release by damaged tissues, the subsequent dilatation of their blood vessels, and the localized pooling of blood. Anti-inflammatories all act to counter these processes, hence reducing tissue swelling and facilitating quicker healing.

Side-effects are varied and often quite damaging in themselves. They include 1) peripheral edema 2) potassium loss 3) increased calcium excretion 4) muscle weakness 5) osteoporosis 6) protein catabolism 7) constipation 8) abdominal pain 9) heart burn 10) diarrhea 11) drowsiness 12) tinnitus 13) dizziness.

Generic Label: aspirin

Trade Label: 1. Bayer
2. Bufferin

How Supplied: 5 grain tablets of 100 per bottle (varies with brand label)

Clinical Dosage: 1 - 2 tablets every 4 hours as needed

1984 List Price: $.85 @ 100 (generic)

Comments: Easily the most readily available (over-the-counter) and inexpensive mode of anti-inflammatory treatment; very effective and relatively harmless, with gastro-intestinal (GI) upset in some individuals; marketed under several trade labels; sometimes enterically coated to circumvent GI upset; should always be considered first before moving on to more hazardous anti-inflammatory therapies; also a potent analgesic.

[illegible] sodium succinate

[illegible]

How Supplied: 100 mg/ml injectable, 2 ml vials (Hydrocort)

25

20 mg tablets, bottles of 100 (Hydrocortisone)

Clinical Dosage: 100 - 500 mg every 2, 4, or 6 hours, depending upon severity of injury

1984 List Price: $3.45 @ 100 (tablets)

Comments: High incidence of connective tissue damage in chronic users of this drug; injectable is less harmful than tablets; should be used as infrequently as possible in athletes.

Generic Label: betamethasone

Trade Label:
1. Celestone
2. Celestone Soluspan
3. Celestone Phosphate

How Supplied: .6 mg tablets, bottles of 100 (Celestone)

6 mg/ml injectable, 5 cc vials (Soluspan)

Clinical Dosage: .6 mg - 7.2 mg daily

1984 List Price: $6.75 @ 5 cc (Soluspan)

$46.75 @ 100 (Celestone)

Comments: Use injectable wherever possible to minimize hazards; potassium supplementation often necessary.

Generic Label: naproxen

Trade Label: 1. Naprosyn

How Supplied: 250, 375, and 500 [illegible] bottles of 100 [illegible]

Clinical Dosage: 250 - 375 [illegible]

1984 List Price: [illegible]

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Comments: Very effective agent whose actions peak within 2 hours; also a [illegible] analgesic.

Generic Label: methylprednisolone

Trade Label: 1. Depo-Medrol

How Supplied: 20, 40, and 80 mg/ml injectable; 1, 5, and 10 ml vials

Clinical Dosage: Lowest effective dosage

1984 List Price: $3.65 @ 10 cc (20 mg/ml generic)

$7.25 @ 5 cc (80 mg/ml generic)

Comments: An effective injectable, but with several associated risks as in other anti-inflammatories.

Generic Label: dexamethasone

Trade Label: 1. Decadron

How Supplied: 4 mg tablets, bottles of 100

4 mg/ml injectable, 1 and 5 cc vials

Clinical Dosage: .75 - 9 mg daily (oral)

.5 - 9 mg daily (injectable)

1984 List Price: $8.25 @ 5 cc

Comments: Very similar in chemical makeup and actions to Celestone.

Generic Label: phenylbutazone

Trade Label: 1. Phenylbutazone

2. Butazolidin

How Supplied: 100 mg capsules/tablets, bottles of 100

Clinical Dosage: 100 - 400 mg daily

1984 List Price: $18.40 @ 100 (capsules)

$4.50 @ 100 (tablets - generic)

Comments: Should be taken with meals to minimize GI upset; also used as an analgesic.

Generic Label: dimethyl sulfoxide

Trade Label: 1. DMSO Topical Ointment
2. Rimso-50 (veterinary grade)

How Supplied: sold by the ounce, or the gallon

Clinical Dosage: lowest effective amount

1984 List Price: commercial grade DMSO produced for less than $1.00 per gallon; sold for upwards of $10.00 per 8 oz.

Comments: Use only medical grade DMSO (or veterinary grade), in order to avoid contaminants; available only in Oregon, Florida, Louisiana, and Nevada through physicians; use dilution ratios of less than 80% in order to avoid skin irritation; extremely effective as an anti-inflammatory agent, but with some risks which might include skin burns, diarrhea, nausea, DMSO breath, headache, and rarely photophobia; use sparingly over injured area, not to be taken internally. (May be combined with aspirin in solution for direct absorption through epidermis)

Analgesics: [illegible]

Analgesics are intended [illegible] pain and [illegible] depending upon the [illegible] inflammatory as well [illegible] side effects [illegible] vary, and sometimes include [illegible] 2) dizziness [illegible]

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3) nausea 4) vomiting 5) sweating.

Generic Label: aspirin (see under Anti-Inflammatories)

Generic Label: acetaminophen

Trade Label: 1. Tylenol

How Supplied: 500 mg capsules (extra-strength), quantities vary per package

Clinical Dosage: 2 capsules 3 - 4 times daily

1984 List Price: $6.95 @ 100

Comments: Popular over-the-counter pain-killer; available under several brand labels; does not cause GI upset like aspirin; does not have anti-inflammatory action; very safe.

Generic Label: meperidine

Trade Label: 1. Demerol

How Supplied: 50 and 100 mg tablets, bottles of 100 and 500

Clinical Dosage: 50 - 150 mg every 3 - 4 hours

1984 List Price: $7.65 @ 100 (50 mg generic)

Comments: Potent narcotic analgesic, actions similar to morphine; may cause severe adverse reactions.

FIRST-AID

How Supplied: 300 mg tablets, bottles of 60

400 and 600 mg tablets, bottles of 100

Clinical Dosage: 400 mg every 6 hours, not to exceed 2400 mg total daily dosage

1984 List Price: $10.60 @ 60 (300 mg)

Comments: Effective within 2 hours; acts as anti-inflammatory agent as well; moderately effective for pain.

Generic Label: propoxyphene

Trade Label: 1. Darvon

How Supplied: 32 mg tablets, bottles of 100

Clinical Dosage: lowest effective dosage

1984 List Price: $8.15 @ 100

Comments: Potent narcotic analgesic; same adverse reactions as Demerol.

Generic Label: dimethyl sulfoxide (see under Anti-Inflammatories)

Muscle Relaxants:

Following severe injury and/or cramping due to electrolyte depletion, many athletes actively seek a form of "relaxation" therapy for affected muscles. This class of drugs attains muscle relaxation by blocking interneuronal activity and has a fairly rapid onset, usually 4 - 6 hours [illegible]

Side-effects may [illegible] dizziness 3) temporar[illegible] 5) confusion 6) dis[illegible]

30

9) hiccups 10) agitation.

Generic Label: soprodol

Trade Label: 1. Soma

How Supplied: 350 mg tablets, bottles [illegible]

Clinical Dosage: one tablets 3 times [illegible]

1984 List Price: $4.65 @ 100 (350 mg [illegible])

Comments: Does not directly relax [illegible] muscles.

Generic Label: dimethyl sulfoxide [illegible] Anti-Inflammatories)

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	20,000 IU	10cc bottle	$35.00	$28.00
CHEQUE DROPS (sublingual drops)	100 mcg/ml	55cc bottle	$30.00	$26.00
Methandriol Dipropionate	50mg/cc	10cc bottle	$19.00	$15.00
Nandrolone Decanoate (DECA-DURABOLIN)	100mg/cc	2cc bottle	$19.00	$15.00
	200mg/cc	1cc bottle	$19.00	$15.00
DECA-DURABOLIN pre-filled syringes (Organon)	100mg/cc	1cc syringe	$12.00	$10.00
	200mg/cc	1cc syringe	$22.00	$17.60
Nandrolone Phenpropionate (DURABOLIN)	50mg/cc	2cc bottle	$10.00	$ 8.00
Testosterone Cypionate (DEPO-TESTOSTERONE)	200mg/cc	10cc bottle	$19.00	$15.00
Testosterone Enanthate (DELATESTRYL)	200mg/cc	10cc bottle	$19.00	$15.00
Testosterone Propinate	100mg/cc	10cc bottle	$12.50	$10.00
	100mg/cc	30cc bottle	$30.00	$24.00
Testosterone Suspension Aqueous	50mg/cc	10cc bottle	$ 7.00	$ 5.60
	100mg/cc	10cc bottle	$ 9.00	$ 7.20
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	50mg/cc	10cc bottle	$32.00	$29.00
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	50mg/cc	10cc bottle	$35.00	$32.00
WYDASE	150 USP/cc	10cc bottle	$13.00	$10.40
Liver Injection (refined)	20mcg/cc	10cc bottle	$ 5.00	$ 4.00
(crude)	2mcg/cc	30cc bottle	$ 5.00	$ 4.00
Fero-B-12-Forte Injection; each cc contains; Liver 20mcg, Iron 60mg, Niacinamide 50mg, B-2 0.05mg, B-6 0.05mg, B-12 15mcg.		30cc bottle	$ 8.00	$ 6.40
Vitamin B-12 Injection	1000mcg/cc	30cc bottle	$ 6.50	$ 5.00
B-Complex Injection with Vitamin C		10cc bottle	$ 5.00	$ 4.00
DURABEX-34 E--Amino-Acid-Vitamin Supplement		500cc bottle	$10.00	$ 8.00
Monoject Syringes 3cc 22 gage 1", 1 1/4", and 1 1/2"		package of 10 syringes	$ 3.50	$ 3.00
		box of 100 syringes	$26.00	$22.00
Monoject Syringes 3cc 25 gage 5/8" (vitamin syringes)		10 syringes	$ 3.50	$ 3.00
		100 syringes	$26.00	$22.00
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ANAVAR	2.5 mg bottle of 100	$30.00	$28.00
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Furosemide (LASIX)	40mg bottle of 100	$16.00	$12.80
MAXIBOLIN	2mg bottle of 100	$19.00	$15.00
Methandrostenolone (DIANABOL)	2.5 mg bottle of 500	$75.00	$60.00
	2.5 mg bottle of 100	$15.00	$12.00
	5 mg bottle of 500	$150.00	$120.00
	5 mg bottle of 100	$30.00	$24.00
Methyltestosterone Tabs (sublingual)	10mg bottle of 100	$10.00	$ 8.00
	25mg bottle of 100	$15.00	$12.00
Stanozolol (WINSTROL)	2mg bottle of 100	$20.00	$16.00
TRISORALEN (sun tan pills)	5mg bottle of 28	$18.00	$14.40
L-Dopa	500mg bottle of 100	$30.00	$24.00
Tryptophan	500mg bottle of 24	$ 5.45	$ 5.45
	500mg bottle of 100	$17.55	$17.55
Thyroid (Thyrolar)	1gr(64.8mg) 1000 tablets	$12.00	$ 9.60
L-Thyroxine Sodium (SYNTHROID)	.2mg bottle of 1000	$12.00	$ 9.60
Sodium Liothyronine (CYTOMEL)	25mg bottle of 100	$ 6.00	$ 4.80
PROLOID	1 1/2 gr 100 tablets	$ 7.75	$ 6.00
Butagen Tablets (BUTAZOLIDIN) anti-inflammatory	100mg bottle of 100	$10.00	$ 8.00
Carisoprodol Tablets (SOMA) muscle relaxer	350mg bottle of 100	$12.00	$ 9.60
TESLAC	50mg bottle of 100	$53.70	$42.96
NOLVADEX	10mg bottle of 60	$75.00	$65.00
DIAPID NASAL SPRAY	8ml bottle	$25.00	$21.00
HYDERGINE	1mg bottle of 100	$30.00	$24.00
DEANER	250mg bottle of 50	$40.00	$36.00
CLOMID	50mg package of 30	$100.00	$100.00

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	1000 mg bottle of 100	$ 3.25
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Super Purple--multiple vitamin-mineral supplement	bottle of 100	$ 3.25
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Dessicated Liver with B-12	10 1/2 gr bottle of 1000	$10.34
Enzymatic Digestant Tabs (starch blockers)	bottle of 100	$ 3.84
Lecithin	1200 mg bottle of 1000	$18.85
Bilenol Extra-Strength Tablets (generic Tylenol extra-strength)	500mg 100 tablets	$ 1.50
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Vitamin E Cream, natural	3000 IU 2 ounce container	$ 2.30
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(currently available are Updates on [illegible] Human Growth Hormone)

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Chapter I

Basic Endocrinology and Pituitary Malfunction

AUTHORS' NOTE: In order to better understand the various applications of Human Growth Hormone (HGH), it is important to first look at the endocrine system and understand how it works. The extreme delicacy of this system, and its total dependence on precise amounts of its secretions, warrant utmost caution when tampering with its mechanisms. Any use of human growth hormone should be done only under the strict supervision of a qualified physician.

The endocrine system is composed of a large group of ductless, glandular tissues that secrete "chemical messengers" directly into the blood. These messengers, called hormones, regulate and integrate a variety of bodily functions, and are largely responsible for maintaining a constant internal homeostasis (i.e. the state of equilibrium in the body with respect to various functions and to the chemical compositions of the fluids and tissues, such as temperature, heart rate, blood pressure, blood sugar, etc.). They accomplish their tasks by signaling responses from specific organs and tissues which are conditioned to react to minute amounts of

100

them. The specific characteristic of the endocrine gland which distinguishes it from other glands, is the fact that its secretions are released directly into the bloodstream, affecting only certain tissues which are programmed to respond to a specific hormone. The testis, for example, are endocrine because they secrete sex hormones directly into the blood to be distributed throughout the body, producing a variety of effects, but only affecting "pre-programmed" tissues. Even when the intended destination is near the endocrine gland, the hormone may still travel throughout the entire bloodstream.

In contrast, an exocrine gland will work specifically on a localized area near the gland itself. Saliva, for example, is secreted directly from the salivary glands onto its intended surface, the tissues of the mouth. Wax from the sebaceous glands is released directly into the ear, and tears from the lachrymal glands are secreted directly into the eye. Exocrine secretions are delivered to an epithelial surface by means of a duct, opposed to the endocrine gland, which is ductless.

Several glands, though, may be called both endocrine and exocrine. The pancreas, for example, produces digestive juices and delivers them down a tube into the intestine. However, the pancreatic cells responsible for controlling amounts of blood sugar have a much more difficult job. They need to influence cells in other parts of the body, varying their rate of sugar use or conservation so they produce a hormone called insulin and secrete it into the blood stream in an endocrine fashion. Then, when they detect an excess of sugar in the blood, they can produce more, instantly signaling all relevant tissues needed to take sugar out of circulation.

To further understand the functioning of the endocrine system, we must first turn our attention to the pituitary gland and a region of the brain called the hypothalamus. The pituitary, or hypophysis, is commonly called the "master gland", because it is the relative control center of the entire endocrine system. About the size of a pea, the pituitary is located beneath the hypothalamus in a body cavity at the base of the skull. The pituitary gland is divided into two separate sections, the anterior and posterior lobes. The anterior lobe, or adenohypophysis, secretes at least six different hormones and is controlled by hormone-like "releasing factors" which are delivered through a special blood vessel link from the hypothalamus. The posterior lobe, or neurohypophysis, secretes two hormones, both of which are synthesized in the hypothalamus and later transported to the anterior pituitary lobe, where they are stored before being secreted.

Four of the six hormones produced by the adenohypophysis are tropic (or trophic) hormones; i.e. they regulate the action of other glands within the endocrine system. TSH (thyroid stimulating hormone), for example, stimulates activity of the thyroid gland, upon command through a complex bio-feedback network. ACTH (adrenocorticotropic hormone) controls the secretions of corticosteroid hormones from the adrenal glands, such as aldosterone, which in turn regulates electrolyte metabolization (salt balance). FSH (follicle stimulating hormone) and LH (luteinizing hormone) are both gonadotropins; hormones that stimulate the testes and ovaries (gonads) to release their hormones, and either sperm or ova. Another pituitary hormone, prolactin, stimulates the production of milk after childbirth and the production of progesterone from the corpus luteum in the ovary.

The hypothalamus is a region in the forebrain in the third ventricle and is linked with the thalamus above, and the pituitary below. It contains several important centers controlling body temperature, hunger, thirst, water balance and sexual function. It is also directly connected with emotional activity and sleep. When the hypothalamus receives input from all parts of the body, including the emotional centers of the brain, it administers the necessary actions. For instance, if it detects there is a need for more cortisol, it produces a corticotropin-releasing factor; this stimulates the pituitary to release some of its ACTH, which in turn triggers the release of cortisol from the adrenal glands. In some cases, as with growth hormone (GH) and prolactin, there is an inhibiting factor, which the hypothalamus releases when it requires the pituitary gland to release its output.

Three of the pituitary hormones play a slightly more significant role than the rest, since their effects are more direct than the tropic hormones.

GH (growth hormone), for instance, promotes long bone growth in the limbs and increases protein synthesis. Although it plays its most important role until about age 20, it works on many systems of the body and its effects don't stop after adolescence. GH encourages the growth of cartilage at the ends of the bones. This cartilage forms the matrix for new bone to be laid down. Besides increasing the rate of protein production by the body's growing cells, it increases the amount of energy giving fat and the sugar in the bloodstream.

In many of its effects, growth hormone interacts with other hormones, such as insulin, which regulates blood sugar by instructing body cells to vary their secretion of glucagon. Though at various times the thyroid and sex hormones share a growth-promoting role, the overall effect of GH is seen when its secretion is abnormal. Too little is occasionally a cause of dwarfism — today preventable by GH treatment, while too much causes a person to grow to an abnormal height and to have a distorted bone structure.

The functions of the two posterior pituitary hormones are more specific. ADH, or antidiuretic hormone, is responsible for the regulation of water loss in the kidneys. (Diuresis is the increased secretion of urine by the kidneys, opposed to antidiuresis which is the increased reabsorption of water by the kidneys.) In stage one of urine production in the kidneys, a large amount of water, along with the waste products for excretion, are skimmed off the blood. If that first mixture were to be excreted as urine, too much water would usually be lost. Therefore, at stage two, a different part of the kidneys reabsorbs some of thw water, leaving the eventual urine less dilute. Under the influence of ADH, the kidney will reabsorb a large amount of water. If, on the other hand, the body contains too much water, this situation will be assessed by the pituitary to release less ADH. With its reabsorbing system receiving less stimuli, the kidney will allow more water into the urine.

The posterior pituitary hormone, oxytocin, plays a major role during childbirth and breastfeeding. Oxytocin, during labor, causes the uterus to contract, while at the same time the uterine wall becomes especially sensitive to the hormone. Many women have their labor assisted by injections of oxytocin.

In breast feeding, oxytocin stimulates the ejection of milk from the breasts. The child's sucking stimulates the nerves in the breast, which are linked to the hypothalamus. The hypothalamus in turn, sends a message to the pituitary to release more oxytocin into the bloodstream. Upon reaching the breast, the hormone causes milk to be forcibly ejected from the nipple.

Rivaled only by the nervous system, the endocrine system is one of the most complex examples of nature's genius and provides us with a dependable regulation system. Its precise dependency on checks and balances within itself, raises questions as to the safety and the intelligence of unnecessarily interfering with such a balance.

Pituitary Malfunction

Precise endocrine function is imperative in the development and maintenance of a "normal" human state. The human organism is almost totally dependent on exact amounts of hormones to stimulate and inhibit specific functions. A malfunction in the hormonal network may result in any number of grotesque, often life-threatening impairments.

In some human beings, the pituitary gland functions abnormally. The results of such malfunctions are often tragic. Conditions of extreme stature, such as giantism and dwarfism, are usually the result of the over or under production of growth hormone(GH) by the pituitary. The treatment of such conditions are often extremely difficult, because of the relative inaccessibility of the pituitary and the scarce supply of human growth hormone (HGH). Only within the last decade has science developed techniques to assure some degree of success in inhibiting overactive growth hormone production. This is usually done using any number of surgical radiation or chemical techniques. Underproduction of natural HGH by the pituitary can also be controlled, but a critical shortage of HGH limits the number of patients who may receive treatment. This shortage, brings an important point to light — body builders who purchase this substance are exhausting a finite supply of a substance which could ultimately mean the difference between a normal and abnormal life. Every time a body builder uses HGH as a shortcut to a greater physique, he is potentially denying this precious substance to growth hormone-deficient children. This is not our opinion, as that is not the purpose of this report, this is fact. We feel that any body builder who considers use of this hormone, should be aware, first, that he may be denying another person a chance to live a normal life.

Though dwarfism has appeared throughout history, not until recently was it possible to distinguish pituitary dwarfs from other types. Pituitary dwarfism, unlike other types of the condition, is usually not accompanied by any other deformations. In almost every way, excluding his stature, the pituitary dwarf is a normally-formed human being. This was the case with a pituitary dwarf named Frank Hooey. When Frank was born, he appeared to be a normal infant. But it soon became clear that his rate of growth was far behind schedule. By the time he reached 17, he was only 4'3", the height of an average eight year old.

In 1958 he was directed to pioneer endocrinologist, Dr. M.S. Raben, who was reporting phenomenal results in treating pituitary dwarfism with HGH. After five years of treatment, an exciting metamorphosis had occurred. Frank had been transformed from a pituitary dwarf into a normal-sized young man. Fortunately, the epiphysial ends of a pituitary dwarf's bones do not fuse (i.e. the hardening of the bones that accompanies sexual maturity and inhibits further linear growth) at a normal age, so it was possible for Frank to grow at an age when most adolescents have stopped. To accomplish this miraculous "change of life", Dr. Raben administered three mgs. of HGH, three times a week for five years. During this time, over 15½" were recorded. Aside from a slightly stunted sexual maturity (which was accelerated and corrected with testosterone propionate), Frank had developed functionally and proportionally into a normal man. There were no noticeable side effects attributed to the HGH therapy.

Extracting of HGH

There are probably about 10,000 pituitary dwarfs in the U.S. alone, many who could greatly benefit from HGH therapy. But the supply of HGH is extremely low, since it can only be obtained from human pituitary glands removed at death. Theoretically, an ample supply of HGH could only be obtained if the pituitary glands of three fourths of all those who died annually were collected. This is about two million more than the 80,000 pituitaries which are presently being collected annually.

The method in which the substance is extracted is called the "glacial acetic acid extraction method". Approximately four mgs. of HGH are extracted from each gland. Research has looked into the possibility of utilizing animal glands as a source of growth hormone, but due to what is called **species specificity**, the substances do not have the same effect. Recently, Rhesus monkey hormone has been considered as an alternative, but since its use is accompanied by a variety of skeletal abnormalities, it cannot be used safely.

The needs of children who are afflicted with pituitary dwarfism vary; but on the average, a five year program of HGH treatment may require up to 3000 mgs., an amount that calls for the processing of over 750 pituitary glands!

Giantism and Acromegaly

Giantism, the counterpart to pituitary dwarfism, may be defined as excessive growth in height, greatly exceeding the average for that person's race. Earlier authors concluded that giantism was due to hyperpituitarism (excessive production of anterior pituitary hormones) during the period of growth before the epiphysial ends had fused, and that the same situation caused acromegaly in adults. Patients with giantism often have manifestations of acromegaly also, if the excessive growth stimulus (HGH) were continued beyond the period of epiphysial closure. Occasional patients develop both acromegaly and giantism before epiphysial closure, probably owing to the stimulation of both longitudinal and appositional bone growth. Because growth in the length of bones is possible, giants, unlike acromegalics, may retain normal proportions. The increased growth is gradual and may begin at infancy, proceeding at a fairly constant rate and not stopping until the onset of sexual maturity, when the epiphysial ends fuse. Final height is usually between 7 and 8 feet, (although greater heights have been reported, as in the case of Robert Wadlow, the "Alton Giant", who was measured at a height of 8'3¼" when he died at age 22). Treatment of giantism is similar to that of acromegaly. Both conditions usually warrant the surgical removal of the pituitary or the unplantation of radioactive materials into the pituitary fossa. Unfortunately, though, most cases of giantism usually present themselves after it is too late for treatment to control their height.

Acromegaly was the first pituitary syndrome to be recognized. It was described and named by Pierre Marie in 1886. Soon after, it was generally recognized that the somatic overgrowth was usually associated with a pituitary adenoma and that the condition was due to the overproduction of GH by pituitary tumor cells.

Acromegalic manifestations are the result of the effects of hypersecretion of GH by the pituitary gland and from pressure by an expanding tumor on neighboring sites. The condition generally develops gradually and the patient usually does not seek medical attention until the condition is well marked. The following presents any one of numerous manifestations which may accompany acromegaly.

1. enlargement of the skeleton and viscera
2. obvious enlargement of hands and feet
3. enlargement of nose and lips
4. coarsening of facial features
5. thickening of skin, with developing corrugated furrows
6. enlargement of sebaceous glands, hair follicles and sweat glands
7. enlargement of tongue and nasal sinuses
8. Osteoporosis (demineralization of bones, causing them to become brittle and to break easily
9. Arthritis
10. loss of menstrual cycle in women, loss of libido and impotency in men
11. Diabetes
12. heat intolerance, excessive perspiration
13. headaches

Acromegaly is an extremely ravaging and insidious affliction. Without warning, it can take a normal man or woman and cause total cosmetic disfigurement, along with the aforementioned list of potentially more serious manifestations. As with giantism, surgery or radiation therapy are the primary means of inhibiting excessive GH production and in turn halting the affliction. In order to prevent disfigurement, however, treatment must be performed before irreversible ugliness supervenes.

Chapter I Notes

Chapter II

Growth and Growth Hormone

Growth

A human being starts life as a single cell, that through almost infinite cell division, becomes an organism whose body is made up of trillions of cells. From this single cell develops an almost endless variety of specified tissue: muscle, bone, organ and blood, to name a few.

This process, which may be referred to as growth, involves three criteria:

1. protein synthesis and accumulation;
2. lengthening of long bones;
3. increased cell division.

In man, two rapid periods of growth occur: one during the first two years of life, and the other during adolescence (see fig. 2-1). It is interesting to note, however, that total and linear somatic growth is not indicative of growth rate of specific organs (see fig. 2-1). At present, very little is known about the relative individual organ growth rates.

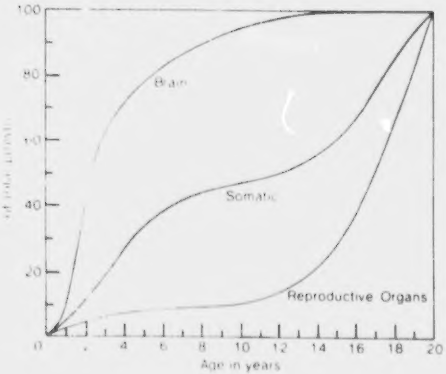

Fig. 2-1 Relative growth rates of the brain, body (somatic) and reproductive organs.

Another important implication of differential growth rates is that the so-called periods of development vary from organ to organ. Thus, a period of sickness or malnutrition during infancy (during the major period of brain growth, see fig. 2-1), may cause irreversible brain damage, whereas the reproductive organs may be unaffected.

Growth capacity is genetically predetermined, however, there is no guarantee that maximum growth will be attained. Attaining maximum capacity is primarily contingent on:

1. an adequate supply of vitamins, minerals and the essential amino acids.
2. freedom from disease and sickness.
3. an adequate supply of fatty acids and calories.

A variety of studies have revealed that the growth inhibiting effects of malnutrition are most profound when they occur early in life. Malnutrition during infancy may cause the irreversible stunting of somatic growth, since the first two years of an infant's life are the most crucial somatic growth period. There is also a strong possibility that pre-natal malnutrition may have a profound effect on somatic growth; but at present, there is not sufficient research to substantiate this.

Sickness can stunt growth, probably because cortisol and other related factors enhance protein catabolism. If the illness is temporary, the child may manifest an extreme "growth spurt" upon recovery; and while the mechanisms which are responsible for this phenomenon are presently unknown, the process clearly demonstrates the precision of a genetically-determined sequence.

The Effect of GH on Growth

Removal of the pituitary gland in young animals stops the linear growth process. Conversely, the administration of large amounts of GH to young animals causes abnormally excessive growth. When excess GH is given to adult animals whose epiphysial ends have fused, not allowing further linear growth, it causes the disfiguring bone thickening and overgrowth of other organs (acromegaly).

100

The growth promoting effects of GH on organic metabolism are primarily due to its ability to stimulate protein synthesis. It does this by increasing membrane transport of amino acids into cells and also by stimulating the synthesis of RNA, two events essential for protein synthesis. GH also promotes large increases of mitotic activity and cell division, the remaining primary components of growth.

The effects on bone are extensive. Bone is a living tissue which consists of a protein matrix upon which calcium salts are deposited. The cells which are responsible for laying down this protein matrix are called osteoblasts. Growth of long bone depends on actively proliferating layers of cartilage at the ends of the bone. The osteoblasts at the edge of the cartilage convert the cartilaginous tissue into bone while new cartilage is being formed simultaneously. GH induces this lengthening by promoting protein synthesis in both the cartilaginous center and bony edge of the epiphysial plates, as well as by increasing the rate of osteoblast mitosis. These effects on bone growth are not directly stimulated by GH, but by a substance called somatomedin, which GH causes to be released by the liver and probably kidneys.

Growth Hormone

Structurally, human growth hormone is a single-chain peptide containing 190 amino acids, its molecular weight is 21,500. Within the substance of the gland and in the plasma, human growth hormone (HGH) is heterogeneous. Orthodox HGH (the 21,500 peptide), has in common with placental lactogen and prolactin several intervals of identical amino acid sequence. Human growth hormone is produced by the pituitary in amounts not exceeding 500 micrograms per day.

The conspicuous action of HGH is anabolic (i.e. pertaining to the constructive phase of metabolism whereas foodstuffs are converted into living tissue). Tissue protein is stored in amounts greatly exceeding the quantities that can be accounted for by the amount of new tissue formed. This new mass that is provoked by HGH, is not accompanied by fat deposition. In fact, HGH has been shown to accelerate fat metabolization. Acromegalics, for example, are very rarely obese.

The serum concentration of HGH has been shown to be extremely flexible to a variety of stimulus. HGH is spontaneously released in periodic "bursts" directed by the central nervous system. Deep sleep, fasting and intense exercise trigger a distinct rise in serum values, (though in some obese individuals these responses are stunted). Disease and sickness also stimulate the release of HGH, as do various types of stress and trauma. The infusion of various amino acids (i.e. L-dopa, arginine, ornithine) has shown to be particularly effective in stimulating the release of growth hormones. Glucagon, ACTH (adrenocorticotropic hormone), and catecholamines trigger a similar response (also see Chapter 5, Growth Hormone Releasors). Chlorpromazine and somatostatin have an inhibiting effect on growth hormone release.

Chapter II Notes

Chapter III

Drug Evaluations of GH

Before GH therapy is implemented, a criteria for treatment must first be established. Patients must first show significant short stature and/or a retarded growth rate. Patients with congenital GH deficiency should be below the third percentile for height and growing at a rate of 5.0 cm a year.

Evidence of pituitary malfunction resulting in a somatotropin (GH) deficiency, is usually demonstrated by at least two of the following stimulation tests:

a. insulin hypoglycemia test
b. intravenous arginine tests
c. oral levodopa tests

Although antibodies may develop which neutralize the therapeutic affect of GH, therapy is effective in more than 95% of the cases treated.

Anabolic steroids are occasionally administered with GH in an effort to conserve the dwindling supply of GH. Recent research has linked somatic growth (specifically linear) stimulation to the concomitant implementation of these two substances, although ample research has not been done to confirm this. Questioning the superior effectiveness of anabolic steroid growth hormone combinations, a particular study (Rosenbloom et al. 1980) utilized GH therapy alone. Using weekly injections of 2.5 I.U., the growth response was at least as great as the results achieved with the anabolic steroid growth hormone combination.

GH therapy is usually not effective in patients whose bone age exceeds 16 years, whose epiphysial ends have fused, or whose production of somatamedin is not affected by GH administration (see Chapter II). It should be noted, however, that there are exceptions to this rule, and that successful GH therapy has been made in patients whose bone age well exceeded 16 years, but this is rare.

Precautions

Growth hormone is diabetogenic (i.e. it causes diabetes). It should be used with extreme caution in patients with diabetes mellitus or with a family history of diabetes mellitus. It will augment an existing diabetic condition, and it may bring about diabetes in individuals whose family history demonstrates diabetes. Keep in mind that this is a precaution when treating a pituitary-deficient child, as the risk certainly outweighs the alternative; but as for a diabetic bodybuilder whose GH levels are normal, this is not a precaution, but rather a direct warning not to use this substance. In this case, the risk absolutely outweighs the benefit.

Hypothyroidism may also develop as a result of GH implementation. Patients should have periodic thyroid tests administered and be treated with thyroid hormone when indicated.

Subcutaneous administration of GH may lead to a condition called lipodystrophy, whereas a disturbance in fat metabolism occurs, causing the subcutaneous fat at the site of injection to disappear (the fat in surrounding areas remains unaffected). GH must be administered intramuscularly and the site of injection should be rotated.

Bone age should be monitored annually, especially in patients who are pubertal and/or are receiving concomitant thyroid therapy. Under these conditions, epiphysial maturation may be accelerated. GH therapy will induce little or no affect on linear growth after maturation has occurred.

Side Effects

Growth hormone, as discussed earlier in this chapter, may cause the formation of antibodies which render the GH neutral. Although occurrence of this "neutralization" is rare, 5% of all patients fail to respond to treatment.

It is also noteworthy to mention that hepatitis and AIDS may be contracted through use of growth hormone. Because GH is extracted from the pituitaries of cadavers, there exists a possibility for this to occur. If the donor of the pituitary had AIDS, but was unaware of its presence before he died, this could be passed on through the GH. Although there are no reported cases of this as of yet, the prevalent epidemic potentiality of AIDS may soon change that.

Excessive levels of GH will cause a distinct, rapid thickening of the skin, which is usually reversible upon discontinuance of the drug. Excessive levels of GH can cause a lowering in the voice pitch (due to larynx enlargement), the irreversible enlargement of joint diameter, as well as a variety of other skeletal abnormalities. It is extremely important that initial therapy does not exceed the recommended therapeutic dosage. Then upon assessment of the patient's progress, dosage adjustments may be made.

Recently a growing number of disturbing cases of GH abuse have brought about a variety of side effects. Keep in mind that almost all research into the effects of GH therapy has been specifically done utilizing the replacement of GH in deficient individuals.

Research has not warranted the use of GH in individuals who already possess normal levels. A bodybuilder in Philadelphia noticed a distinct thickening of the skin and coarsening of his facial features which he attributed to use of the drug. (He received 2 I.U. of Asellacrin®, three times a week, for six weeks, intramuscularly. This dosage, incidentally, did not exceed the recommended therapeutic dosage.) Upon discontinuing "treatment", his skin thinned, but he still claimed to "look different", though he could not specify how. Upon viewing a photograph of an acromegalic, he immediately paralleled his "look" as a mild form of acromegaly (see Chapter I). Although the authors of this book did not make the same association, he "swears that there was a change in his facial features, taking on slight acromegalic form". Even though science has not yet documented many cases of drug induced acromegaly, it should be mentioned that the authors of this book have interviewed several persons who claim to have developed cosmetic changes in their facial and somatic features. It is definitely not out of the realm of possibility to experience such changes due to GH administration. After all, acromegaly is basically nothing more than the hypersecretion of GH in an individual whose linear growth is complete. Bodybuilders should be aware that the use of GH as a physique enhancer is new and adequate research has not yet been made to substantiate the safety of implementing the substance to normal individuals. What it narrows down to is a personal decision, based on a benefit to risk ratio. But until more research is done, an accurate assessment of such a ratio will be impossible.

Therapeutic Dosage and Administration

GH administration, as discussed earlier, must be IM (intramuscular) only. Individual dosages may vary, but therapy usually begins at 2 I.U., 3 times per week (48 hours must pass between injections). It may be necessary to increase the dosage in older hypopituitary children, particularly if sexual maturation is delayed. After long periods of treatment (2 or more years), growth rate may decline. Withdrawal for 2-3 months may rejuvinate the growth response upon resumption of treatment.

If, during continuous therapy, the rate of growth slows below 1 inch during any six month interval, the dose is usually doubled for the next six months. Upon reaching satisfactory adult height, when the epiphysial ends have fused, or when treatment is no longer effective, GH administration is discontinued. The cost for one year of treatment ranges from $4,500.00 to $9,000.00, depending on the regimen. The high cost of GH is indicative of its relative scarceness. Growth hormone is available as follows:

Asellacrin® (Serano Laboratories)	**Crescorman®** (Pharmacia Laboratories)
Powder for Injection: 2 I.U. per vial[1] in 2 ml vials with diluent. 10 I.U. per vial[2] in 10 ml vials with diluent.	**Powder for Injection:** 4 I.U. per vial with 2 ml diluent.
[3] $200.00 per vial	[3] $100.00 per vial

[1] With 20 mg mannitol

[2] With 40 mg mannitol

[3] As of August 1983

Chapter III Notes

Chapter IV

GH in Bodybuilding

If bodybuilders were as muscular as they are misinformed, a twenty-nine inch arm would probably be considered small. This became evident during a series of extensive interviews we conducted with bodybuilders of all levels, during early 1983. Most bodybuilders, when referring to drugs, (and training, for that matter), are suffering from the same condition – ignorance. The interesting thing we discovered was that bodybuilders were not only misinformed, but they were, for the most part, misinformed with the same information. (If someone discovers the method used to distribute this "misinformation", and applies it to correct information, we'd be in great shape!) But of all the myths we encountered through our interviews, none were more ridiculous and dangerous than the ones which manifested human growth hormone in bodybuilding.

1) Most bodybuilders believe that HGH is some sort of a miracle drug with no side effects, a "build-all" panacea which is completely safe. This is simply not true. Known side effects range from a temporary thickening of the skin to the permanent overgrowth of the skull and joints (also see Chapter III). And because of the relative newness of the drug in this application, ample research has not been done to determine the extent of the side effects associated with this substance. Bodybuilders who use HGH, risk suffering from any one of the known side effects, as well as an unknown, potentially more dangerous one.

2) Another popular misconception is that HGH stimulates the muscles to grow without exercise. This myth probably stems from the fact that HGH does induce an extremely slight amount of muscle tone without exercise, in individuals whose musculature is atrophied. However, in individuals whose muscles are developed to any degree, the drug will not be effective without heavy resistance training.

3) The misconception that HGH is an affordable and readily availabe substance is probably one of the most ironic. The fact is, HGH is in critically low supply, as its only source is the pituitary glands of freshly dead cadavers. The substance is in such short supply that many growth-deficient children are not receiving adequate treatment. The extraction of HGH is time consuming and expensive, accounting for the astronomical prices which the substance commands. Bodybuilders who plan to receive treatment, can plan on spending anywhere from $350.00 to $600.00 a week. An eight-week treatment could cost up to $5,600.00, not counting doctors fees or clinical tests! The drug also must be purchased with a prescription. There is some of it on the black market, but this is definitely not recommended. We have seen several substances which were being sold as HGH, which they were not. One dealer was selling a form of GH derived from monkeys. He claimed it was safe and effective. The fact is that this form of the substance will cause a gross disfigurement of the skull and bones – it is totally unsafe. Other black market dealers sell what they call a "pre-mixed solution of GH." Upon examination, we identified their "pre-mixed solution" as normal saline solution; it is totally useless. In fact, out of the fourteen dealers we spoke with, only one was selling the real thing. It's only common sense to conclude that black-market dealers just can't get the substance. Some doctors can't even get it for patients who critically need it! If a black-market dealer does have it, then where does he get it? Does he extract it from corpses himself? Probably not. Chances are the majority of GH being sold illegally is not the real thing. Anybody who is naive enough to purchase GH on the black market is literally laying his life on the line. If you feel you must use growth hormone, get it from a physician. As far as we are concerned, this is the only way to do it.

HGH and Muscle Growth

AUTHORS' NOTE: This section of the chapter primarily deals with the feedback we have received during interviews with physicians and bodybuilders who have had experience with HGH, and its other than therapeutic applications. Although a number of reports of phenomenal gains without side effects have been made, the lack of research into this application of the drug has not yet substantiated these reports. Thus, the interviews and reports which follow are not intended to be taken as scientific fact. Until more research is done, bodybuilders should exercise extreme caution when dealing with this substance. Any use of this drug should be done only under the strict supervision of a competent physician.

A 32-year-old male bodybuilder reported "exceptional muscle gains with a loss of bodyfat and no noticeable side effects" during an eight-week period which he used 4 I.U. of Asellacrin® (Serono) three times a week (on nonconsecutive days). He said that he preferred the HGH over anabolic steroids, because he developed gyne-

comastia (development of the male breast), with the steroids, but did not with the HGH. He also stated that he felt the cost of the HGH (about $3,200.00 in this case) outweighed the gains. He used protein and vitamin/mineral supplements during the eight weeks and trained using a split routine, training every body part three times a week with light-moderate weights. He said that if he "hit the lottery, he would consider using the substance again".

A 24-year-old female bodybuilder claimed "a sufficient improvement in her physique" as a result of her using the drug. She reported an extra half inch on each arm, with each other bodypart responding proportionately. She also reported her bench press going from 75 to 135 during the two months she used the drug.

When asked about side effects, she said that her skin had become thick and course, and that the pitch of her voice was lower than before she used the drug. She said she did not mind these side effects and would continue using the drug, as long as she could afford it. She was using 2 I.U. three times a week. She trained three times a week, hitting all bodyparts each time.

A California physician reported "great results" in over fifty individuals to whom he was prescribing the drug. He claimed that the drug had not induced any noticeable side effects in the individuals he was "treating". He said he usually prescribed 6 to 12 I.U. per week, depending on an individual evaluation of the client. He reported "vastly greater gains using the Crescorman® (Pharmacia) brand of the drug, over the other brand, Asellacrin® (Serano)", for reasons he could not determine. He viewed HGH as a logical and safe alternative to anabolic steroids, but stated that he did not feel that anabolic steroids were "that unsafe if used properly". When asked about the shortage of HGH and how it might affect the future of individuals who are growth deficient and need the substance, he said he "believed there was no longer a shortage".

A 22 year old male bodybuilder used 4 I.U. of Crescorman® three times a week and reported "decent gains". He said, "although he felt that he had grown while using the drug, the cost much outweighed the gains". He used the substance for 10 weeks, but did not notice any gains until the fourth week, when he started administering the drug at night, rather than the morning. He claims that switching the time he administered the drug made 100% difference and that the drug is virtually useless if administered in the morning.

He used a high-intensity workout style which he attributed to the degree of his gains. He said he did not "notice any side effects, except a particularly empty feeling in his wallet".

A 39 year old weight trainer experienced "good muscle development and great fat reduction", which he attributed to the drug. He said he noticed no side effects and would continue using the drug until he attained "maximum development". He used 4 I.U. of Asellarin® three times a week for the first month and 6 I.U. for the next two months. He claimed the drug made him feel stronger and younger, and he was now able to work out harder and longer than he had ever done before, and he highly recommends that other athletes try it.

Obtaining HGH

For those individuals who feel they have to use HGH, and will do so, no matter what the facts may be, there is only one way that such use can even be considered. A competent physician is the only source where an individual can logically consider obtaining HGH. However, before your doctor can give you a prescription that may be intended for non-FDA (Food and Drug Administration)-approved use, he or she must ascertain that research warrants it. You can help your physician and yourself by becoming intimately familiar with all aspects of such usage.

Though it is legal for doctors to prescribe any substance for any purpose (except for controlled "drugs of abuse" such as narcotics, stimulants, sedatives, etc., and specifically-banned substances as Laetrile), there may be several reasons they have for denying you a prescription.

1. The doctor thinks you may be careless and ignorant of the drug's potential adverse side effects.
2. The doctor may be concerned about a lawsuit for prescribing a drug for non-FDA approved use.

If, after thoroughly researching and understanding all aspects of HGH use (read this book cover to cover), an individual still wishes to use them, there are several ways to respond rationally to your doctor's objections.

The best way is to arm yourself with adequate knowledge. Basically, the doctor is concerned that you will get yourself into medical trouble using the drug and, perhaps also, that he or she will be blamed and sued for malpractice. If the doctor sees that you intend to use the drug in a responsible manner, he will be more apt to consider it. Show him that you intend to be responsible by exhibiting an indepth knowledge of the drug and the potential risks associated with its use.

Read as much as you can before approaching your physician. Buy a copy of the Physician's Desk Reference (PDR), which lists prescription drugs of the United States, along with information about drug safety, including contraindications, dosage and administration, toxicity, side effects, etc. Write to the drug manufacturer, (see Appendix C), and ask for reprints of research papers about the drug in which you're interested. Read as much reliable, credible information as you possibly can; this will assist in his understanding of the drug and its relevant application. In approaching a physician for the first time with this matter, try and demonstrate to him the following:

1. You have carefully researched all aspects of the drug's therapeutic application as well as the FDA non-approved use. (Bring any and all information with you, especially current research papers.)
2. You intend to use the drug in a responsible manner and are aware of the potential dangers.
3. You have made a definite decision to use HGH but prefer to do so under the strict supervision of a competent physician.
4. You intend to have clinical laboratory tests run before and while using them to monitor for possible side effects that you have read about in the research papers and PDR.

If your doctor still will not prescribe the drug, ask for an explanation of his objections. Often you will find that his objections are valid. In other cases, you will find the objections to be based on a lack of knowledge of the FDA non approved uses for the drug. Then, you should give your doctor copies of the relevant information which you have acquired. If he still does not wish to become involved, ask him to refer you to a doctor with experience in this matter, or seek another doctor on your own. Shop around, find a doctor who has knowledge in this area, one who will insure the safest, most productive experience with the drug. If you can locate a doctor who specializes in sports medicine, chances are you will find someone knowledgeable in this area. Using the aforementioned guidelines when aproaching the physician will increase the chance of his becoming involved.

Dosage and Administration

AUTHORS' NOTE: Do not substitute this advice for the advice of your physician, as it is not intended to be a substitute. It is intended to be used only with the supervision of a qualified physician. This is by no means everything a person needs to know about the administration of HGH. Each person is somewhat biochemically individual. There is no way a book can, in the light of this biochemical individuality, safely and effectively recommend exact dosages and methods of administration.

Before using HGH, have any and all applicable clinical laboratory tests conducted. While using HGH, these tests should be periodically repeated. The results of these tests will mean nothing to you; they must be analyzed by a physician. This advice is not a mere formality; we sincerely mean what we say here. Without proper tests, your health and life may be in jeopardy.

The following is a basic guideline to be used with your physician in planning and administering your HGH usage plan:

1. **Dosages should be administered three times a week with at least 48 hours between injections. (Injections must be IM – Intramuscular only.)**
2. **The site of injection should be rotated. (The hip/buttocks area is the preferred site of injection.)**
3. **Maximum growth occurs at a dosage of 0.3 I.U. per kilogram of bodyweight per week. (This amount should be divided into three nonconsecutive weekly dosages.) Exact dosage should be calculated by a physician.**
4. **Injections appear to be more effective when given in the late afternoon or evening.**
5. **Crescorman* (Pharmacia Labs) has been reported to yield better results than other brands of the substance. (This has not been substantiated.)**
6. Duration of use in this application has not been established, though 8 to 10 weeks has proven effective in some individuals. The actual duration, though, should depend on effectiveness, occurrence of side effects and the test evaluation by your physician.

IMPORTANT: For precautions and contraindications, see Chapter 3.

Chapter IV Notes

Mr. **Waxman**. Thank you very much for all of your statements, what we want is a complete report from you. Those bells you heard indicate there is a vote on the House Floor. A lot of things go on at the same time around here. We are going to recess for a few minutes, to run and vote. We are going to go and will be back in 5 to 10 minutes, and then we will want to ask you some questions. We stand in recess.

[Brief recess.]

Mr. **Waxman**. Tam, let me start with you. Can you explain to us why an athlete would use a substance like the human growth hormone when there is no evidence of effectiveness and there's a genuine risk of a disease like diabetes? How difficult would it be to obtain a supply of Protropin from the black market, from your experience? Is it sold like other illicit drugs, where people make money selling this product? Tell us more about that.

Ms. **Thompson**. Well, Mr. Chairman, athletes tend to be adventurous by nature and are not easily dissuaded when they think there is a possibility they can get better. It's like Terry's story about taking the pill that they knew would kill them within a year, even if they knew it would kill them, 50 percent of them would do it. This is something that actually the side effects are not that well known among athletes. They think there may be side effects but they will kind of try anything. They will try any new vitamin supplement that comes on the market. They will try any food. They will try just about anything to get better.

As far as the black market distribution, I was talking to a pharmacy student at the University of Texas and we were trying to figure out how the people I know sell their drugs for approximately one-third of the cost you would pay at even a large chain pharmacy like Eckert's or Walgren's. I said, I know those big chains buy in bulk, how can these little guys selling out of their house and cars be underselling them by a third of the cost. He said, well, I hate to tell you this, Tam, since you have taken this stuff, but I think what is probably going on is they are getting bad lots from pharmaceutical companies that perhaps the pharmaceutical company paid to haul it to the dump or dispose of it or burn it and somewhere along the way, it got sold off.

I might mention I have been clean, drug free, for 2 years and 3 months. I no longer use the stuff. I'm working right now in the American Drug Free Association and doing what I can to try to dissuade people from taking this stuff. I quit taking it myself because I came to the realization that it is cheating. The use of drugs is very widespread in certain areas of the country such as California, Texas, Florida, real hot beds. I have to admit particularly in the Houston area, it's prevalent.

There was a guy that came into the gym I was training at in Pasadena and people pointed him out and said, he's a natural, he didn't take any drugs and people starred at him and they watched him train, it was kind of a new thing.

I got to the national level and the women I was competing against were drug free and they were from Wisconsin, the Midwest. They were talking to me about it. I got to be friends with them. My conscience kind of got to me and I felt guilty and said, well, this is cheating, I can't do this to people that are getting to be my friends, so I just quit doing it.

One of the distributors I knew in the Houston area was a fire fighter. I saw a policeman one time buy some drugs from him in the gym. They would bring their suitcases, usually in my area they brought suitcases in the gym. They had little teflon rectangular sort of boxes with lids that would peel off like you put carrots in in the refrigerator, and they would mark on the box, growth hormone, whatever it was, and they would come in the gym. I've seen them do it right out there on the gym floor when there were not too many people in there.

Mr. WAXMAN. It's very open?

Ms. THOMPSON. Very.

Mr. WAXMAN. Is there a lot of pressure to take these drugs and easy lot of availability to them?

Ms. THOMPSON. I think the pressure, yes, mainly in sports like football and stuff but in power lifting and body building, it's known that if you want to make it to the top, you have to do this.

Mr. WAXMAN. Dr. Kerr, I was impressed that you were able to get this box of Protropin, which was manufactured by Genentech, because they are going to testify later, that the distribution is very carefully controlled. We have been told it is distributed only through hospital pharmacies, 1,000 pediatric and adult endocrinologists, and therefore, we ought to be assured that something like this is going to be distributed only through these channels.

Are these controls working? I guess the answer is not very well if you can pick up a box.

Mr. KERR. It just took $450 and a phone call. As I said, I picked someone who is not a likely drug seller. I could have picked any of 50 or 60 others that I know do sell drugs to athletes. I received letters and phone calls from athletes throughout the country and Canada implying they are taking this drug.

It sounds to me as though there are thousands and thousands of people if not more taking this drug. I don't understand how they are getting it. Somebody is making some money somewhere.

I assume that it is from an inventory in some pharmacy somewhere. We have heard the story, Dr. Todd called me about it, a railroad car in the east that was hi-jacked and someone took the growth hormone out of the car. You know, I've heard that story so many times, when it came to human growth hormone. I mean, at least six times I have heard that story throughout the country. They all said, that's why it's available.

Either there is a very unguarded railroad track back East or it is just a lot of baloney, and I think that is what it is. I think someone is selling this from their inventory and I think that is where we need to find the character.

Mr. WAXMAN. If we move this drug to a controlled substance category, it would certainly make the supply not as available and there would be very strict penalties.

Dr. Taylor, do these penalties work? Is there just too much of an economic incentive to violate the law anyway?

Mr. TAYLOR. First of all, I think you have to look at the fact that drug companies can't make the drug a controlled drug. I think the drug companies are probably doing as much as they can do to limit the illicit distribution. I think the controls work for a particular drug like human growth hormone because there is going to be the technology involved, with manufacturing the drug, it is not something a chemist can do in a garage lab. I think what would specifically work for human growth hormone is in the area of allowing more time for research in clinical settings before we have such widespread use among society. I think that seems to make a lot more sense.

I think it is very easy to cop out and say, well, let's look at other drugs that are on the controlled substance lists, let's look at amphetamines. Amphetamines were a non-controlled prescription drug at one time, until there was approximately five times more amphetamines distributed and used in this country than were being prescribed.

Certainly, it has not totally done away with amphetamine abuse but it certainly stemmed a social tide. The same thing with drugs such as tranquilizers. They were non-controlled general prescription drugs and due to abuse potential and other factors, were moved and reclassified as controlled substances. Certainly, in these cases, the Controlled Substances Act looked very, very good.

When you are dealing with other illicit drugs that can be manufactured in a various number of ways, I'm not sure the situation works, but for a prescription drug as hard to manufacture as human growth hormone, I think it is an ideal situation.

Mr. **Waxman**. One of the arguments we hear against placing human growth hormone under the Controlled Substances Act is that the use of the product does not fit the criteria defined for Schedule II substances. Let me read those criteria to you and see if they fit in this case.

First, does the drug or other substance have a high potential for abuse? I would assume none of you disagree with that criterion for this drug.

The drug or other substance has a currently accepted medical use in treatment in the United States or currently accepted medical use with severe restrictions. That's clear.

Abuse of the drug or other substance may lead to severe psychological or physical dependence. You all agree that is a possibility as well?

If we have those as the criteria for the categorization of this under Schedule II, then this is the kind of drug that could be abused and we want to guard against such abuse.

Dr. Sodeman, let me ask you this question. The College of American Pathologists supports placing human growth hormone under the restrictions of the Controlled Substances Act. Are you at all concerned, as we have heard expressed by some parents of growth deficient children, that such restrictions will prevent ad hoc experimentation by physicians on short children who do not fit the traditional definition of pituitary deficiency? Also would such controls discourage a physician from increasing the dosage of human growth hormone in a patient for whom conventional dosage might not be beneficial?

Mr. **Sodeman**. No. I don't think we have any concern that this will restrict in any way further scientific development on the use of growth hormones in children and other areas in which growth hormone may be useful. All it does is it requires that in fact there be reasonable tracking of that use, tracking that we think is essential in order to avoid abuse and to assure that in fact the physicians are considering that potential, that this is a serious drug, this is a drug they have to be concerned with and therefore, they do have to keep the necessary information.

It also provides a stimulus within institutions in which human testing is being done so that as the committees for human use take and address the issues of the experimental use within university training centers, that in fact they know that this drug is scheduled, it is controlled, and that the necessary recordkeeping will be required as part of the human use experimentation that takes place.

We fully support this. We feel it will not limit in any way the experimentation that will take place in this country and it may in fact encourage it to a certain degree. We think it might encourage it because it will be considered to be a significant drug and the role of that drug is such that it is under the purview of a variety of people so that the use is reasonable and responsible.

Mr. WAXMAN. Mr. Coats.

Mr. COATS. Thank you, Mr. Chairman.

I'd like to ask several questions, starting out with Tam Thompson and Terry Todd and Dr. Kerr, you may want to jump in here, too.

Summarize or capsulize for me the prevailing attitude among athletes in terms of human growth hormone. What is the attitude regarding the side effects, the consequences? Is that just inconsequential? Does everybody just say, don't worry about it, or is the prevailing attitude that there really are no bad side effects, the pluses outweigh the minuses?

Dr. Kerr.

Mr. KERR. At this time, the athletes, I think, are oblivious to side effects.

Mr. COATS. Do they not know or not care?

Mr. KERR. Both. They feel that from what they can gather, there have been no side effects reported in athletes and that is exactly what they want to hear.

Mr. COATS. In other words, the prevailing attitude is there is really not much down side with this particular drug and the pluses far outweigh the minuses?

Mr. KERR. Remember, this drug is not being used just here. This is worldwide in use. In fact, I talked to a Russian athlete last week who seemed to think they were soon to develop a test for growth hormone, Protropin, and they are already developing the blocking agents that they were planning on using to foil its detection.

Also, the use of this drug promotes the use of other black market drugs, because if an athlete takes a growth hormone by itself, he is going to get very little gain, in bulk. He must take another type of anabolic agent and no doubt bought from the black market.

If he is in track and field, he might take one oral agent. If he is a body builder, he might take six or eight different products.

It seems there is something about the ocean air, the closest you get to the beach in Long Beach, along Santa Monica, the greater the use of drugs by these people. You might have athletes, and I'm certain there are many of them, who are taking growth hormone along with a multitude of other anabolic agents.

Mr. COATS. Terry, is that true, is this the prevailing attitude that this is the thing to do regardless of the consequences? How much are the athletes focusing on the long term effects, the potential disastrous consequences of being involved in this mixture and who knows how pure the batch is and what the results are going to be?

Mr. TODD. I think there are several factors that are involved. One is the fact that most of the people about whom we speak are young, quite young. They are much more likely, because of their youth alone, to be risk takers, to be adventuresome, to not feel their mortality, the fact that they are competitive athletes of course moves them another step farther toward the feeling of invincibility. We have to remember that in almost all cases, the people who use human growth hormone are already using a lot of testosterone and other kinds of anabolic steroids and testosterone in particular makes you feel absolutely like Superman, nothing is going to hurt you. As a result of that, you are much more likely to make bad judgments as to what drugs to take, what not to take. You feel as if perhaps other people might fall by the way side to some of these side effects, but in your case, you are simply much too strong and vigorous, potent, virile, tough, and invulnerable so they will never strike you.

It goes with the territory of being at that level. Again, to refer to those two studies, they involved about 100 people in each study. I find them very consequential studies, to demonstrate that if people will die, that suggests to me to warn them they possibly might get some health effects down the line is not going to be very effective if they have already told you they will die in a year in order to be a champion. Therefore, education alone, in my view, is simply not going to solve these problems at all. Some kinds of controls, some kinds of firm testing have to be implemented.

Athletes cannot be convinced by the evidence not to take these drugs.

Mr. COATS. Dr. Voy, you testified that the consequences or possible side effects are decreased muscle capacity, decreased athletic ability. Obviously, this is not believed by the athletes or not experienced by the athletes or they wouldn't keep taking this stuff.

Mr. VOY. Let me coin a phrase that I think Terry used some years ago. The concept here is the unfair predicament that athletes find themselves in, particularly those that have had the opportunity to compete overseas against athletes who do use performance enhancing drugs.

The problem with these drugs are they work. Let's face it. We are not going to lie to anybody. Unfortunately, years ago, 25 years ago, when this all started, the medical profession in its pure ideology stated there was no evidence that these drugs indeed worked. Of course, no athlete would ever accept that, that ever went out and took an anabolic steroid and gained 25 to 30 pounds of lean muscle mass in 8 to 10 weeks and lifted weights 20 to 25 percent more than they had ever lifted in their life.

Now, when we know from the legitimate use of these drugs over the last 25 years in such things as kidney disease, muscle wasting diseases, cancer, et cetera, where the profession has found that the use of these drugs do produce kidney damage, do produce cancer of the liver, do produce premature aging of the coronary and cerebral vascular arteries, now when we turn around and attempt to educate athletes that we know the bad sides, they said, well, doc, you lied to me 25 years ago, when you told me this was a strictly placebo effect.

The profession has lost a great deal of credibility in attempting to educate athletes about the bad side effects. Athletes will use these drugs, if athletes thought you could capsulize horse manure, pardon the expression, in a capsule and take it three times a day, athletes would take that. I am not saying that critical of athletes. I'm simply stating the necessity athletes find themselves in, when they dedicate years and years of their life, their family and everything else to their sport and realize to win, they have to use performance enhancing substances. It is an unfair predicament. They will do it no matter what we attempt to do.

That is one of the reasons why cheating is one of the main objects of the Olympic Committee's drug testing program, to attempt to assure the American public and our sports organizations of fair competition.

Mr. **Todd**. I would have a bought a horse, for example.

Mr. **Coats**. If we go to classifying these as Class 2 substances, I guess the question I have to ask is how effective is this going to be? We have heard testimony from everybody here about the black market offshore sources, people willing to pay any price. If your goal is to become an olympic champion or a national champion, or this, that or the other, yes, it may cost more, because we control it, but it sounds to me like demand is going to drive this thing, and not supply. By restricting supply, we might be able to make it a little tougher to get by increasing the cost. But if somebody's brother-in-law drives the delivery truck or some pharmacist has a friend who is going to make this available, or we've got a doctor who doesn't have any scruples in this area, I think it's just like heroin or anything else. They are controlled substances, but if the demand is there, people are going to find a way to get it. So are we really going to accomplish the purpose that we are after here by controlling this?

Mr. **Kerr**. If that's your only goal, trying to educate the athletes is worthless. But by making the penalties tough for the dealers and for those caught with the drug on their person, I think that is your only control.

Mr. **Coats**. Well, we make penalties very tough for heroin dealers and cocaine dealers, and that doesn't stop——

Mr. **Kerr**. They're not anabolic steroid users. These people are——

Mr. **Coats**. My point is we have made the penalties very tough. We are pouring tens and hundreds of millions of dollars into a drug interdiction effort with very little success. Most of the people in Florida, the Customs agency and FDA, tell me they are lucky if they are getting 10 percent of the stuff coming in from overseas. So I think we might be fooling ourselves here if we think that moving this to a Class 2 controlled substance is going to solve the problem.

Mr. **Sodeman**. But we have to remember that the controlled manufacture status of this particular drug. Many of the narcotics that are available could be manufactured in a variety of places outside of the control of the controlling agents. This drug requires DNA recombinant work, highly sophisticated, high tech work, and the controls can be brought to the manufacturers to try and control some of the access.

Mr. COATS. At least the synthetic manufacturer. Now the human extraction or the extraction out of cadavers, that—we would just go back to the previous system. This was available before it was synthetically manufactured; isn't that right?

Mr. SODEMAN. Right. But I think that market for that purpose as growth hormones will begin to dry up. We will continue to manufacture our hormones from pituitaries for experimental work as we explore other pituitary hormones and the potential use for those hormones. But I do not believe that that market will continue.

Mr. COATS. Are you all in agreement that—excuse me, Mr. Chairman, this is the last question—are you all in agreement that education, the downside, the risk, the long term consequences, really is of no value? That the only method possible of controlling this, and even that is going to be only partly successful, is through controls on the manufacture and distribution?

Mr. TODD. One thing I definitely would like to point out, and I think it's critical, within the last couple of years the FDA, the DEA, and the FBI have been active in the matter of steroids. They have had a big impact. They have put a lot of people in jail. They have had a lot of people under surveillance. It's much more difficult to get certain drugs. The dealers cannot deal with impunity in the way that they have done. This has had a big impact, and I have been told by people highly placed in all those agencies, as well as several of the very major dealers, that one of the things they all agree is that controlling steroids, for instance, and controlling HGH will have a very, very big negative impact on the ability of these drugs to be transmitted as easily as they are now.

Mr. WAXMAN. Thank you, Mr. Coats.

Dr. Voy, do you want to say something?

Mr. VOY. Yes. I just wanted to remind the committee of one thing. We do not have a test for growth hormone. We control the use of anabolic steroids as far as cheating in sports and its abuse in other forms by drug testing. Drug testing has become very reliable, particularly the type of technology that we use at the Olympic Committee and the NC-2A is now using. It's 100 percent. But there is not a test for growth hormone.

So the perception of the athlete out there now is that let's forget the anabolic steroids. We can get the same and better effect from growth hormone, and they can't detect it.

Now studies will show that about 40 percent of these drugs that are gotten are not gotten on the black market. They are gotten from pharmacists and physicians, and putting a substance under the controlled substance, or scheduling it, does one thing, I think, that is very important: It allows us a window of responsibility to, once we find out who the aiders and abettors and suppliers of the drugs are, it gives us the opportunity then to crank in the legal motions that are necessary to take action against these individuals.

So, indeed, I don't possess a lot of confidence sometimes in our laws, in our ability to control the abuse of these substances at the moment. But it does allow us an opportunity, both professionally, to do something about our colleagues who get involved in the business.

Mr. **Waxman**. Dr. Voy, are you saying that the only protection we have would be to place this under Schedule Class II?

Mr. **Voy**. That is the only control I know of at the moment.

Mr. **Waxman**. And therefore do you think we should be taking that action?

Mr. **Voy**. Yes, sir.

Mr. **Waxman**. Mr. Sikorski.

Mr. **Sikorski**. Thank you. It's been helpful.

I'm a little concerned, as I've seen in 10 years of public life, people come in and ask for a magic wand to be waved by the Government, and all of a sudden things will change. I sense that you are not that optimistic. But I'd like to focus on the—whether you have given up on the whole education.

Dr. Voy, is the Olympic Committee working with others, FDA, the Academy of Sports Medicine, in an effort to educate, continue to educate coaches and athletes and parents about the dangers of excess human growth hormone?

Mr. **Voy**. Yes. Let me explain. We began the drug testing program about 3½ years ago, after the expose of the Caracas Pan American games, when our athletes were found to have these substances in their system.

We feel very strongly that drug testing is not a punitive or a police action. It is an educational program. Not one of us here before this committee this morning would be here if it weren't for the drug testing program that was initiated 3 years ago. The USOC uses drug testing as a tool to get the attention of athletes, coaches and administrators as to what this problem consists of.

We have attempted to educate the NFL. I have been involved in consultations with them in their drug program. Obviously you know that Mr. Ueberroth got his experience in the 1984 Olympic games in drug testing with his—as far as professional baseball is concerned, we provided the educational basis, and the training program for the NC-2A or the NCAA to initiate their drug-testing program this fall.

So education is the tool that works, but you need a testing program to exercise that tool, and that's again—I hate to be repetitive, but without a test for growth hormone, that leaves us with an inability to control this substance.

Mr. **Sikorski**. What you are saying is the controlled substance label is educational in itself? It sends a message, it raises a flag.

Can you restate how the Olympic Committee is going to help athletes and coaches avert the potential health hazards of drug misuse, particularly the steroids?

Mr. **Voy**. We spend about $2 million a day on educational programs. We provide a National Drug Control Hotline that is available to coaches, athletes, and to the general public. It's a 1-800 number, in which we answer 7 days a week, 24 hours a day, and on holidays, to provide educational information to individuals requesting it.

We have numerous printed materials. I and our drug testing teams are on the circuit weekly, educating, doing drug testing, giving lectures, et cetera.

Mr. SIKORSKI. We're having a mark-up on eight health-related bills in the Full Committee, so I'll be brief. Now I just wanted to say, I have a friend whose son, a 6-year-old, is about half regular size. In 4 months, he has grown two inches. But the cost is twenty some thousand dollars a year. And what I don't understand—either this stuff is fake, or there's a tremendous mark-up for the actual HGH that isn't prevalent on the black market or the gray market here. They're getting a better deal on the black market, a better price than the parents of the kids that are using it for growth.

Mr. KERR. Well, it costs them nothing to start with, but they steal it, and they can charge anything they like.

Mr. SIKORSKI. If they steal it——

Mr. KERR. I assume that's what is going on.

Mr. SIKORSKI. I assume if something is stolen, there's going to be a report, and I don't buy the idea that it's being stolen in that quantity.

Mr. TODD. There was $250,000 of it that was stolen. It was reported in The New York Times. It was stolen out of a holding facility in New Jersey. That was last year some time. That's a small amount, of course.

Mr. SIKORSKI. That's ten kids, 1 year supply. That's not going to handle the thousands of people we are talking about on a daily basis.

Mr. TODD. I think one thing that everybody here seems to feel is that as the product becomes manufactured by more than one company, not just in this country, but in other countries, that market economics will bring the price down drastically, since the mechanisms used to produce it are not particularly complicated.

The research that went into it was complicated, but the manufacturing process is not overly complicated.

Mr. SIKORSKI. I guess, first of all, they're not getting the same price, they're not paying the same price in the gyms that these parents are paying. It's a lot different price.

Mr. KERR. Another point is that the athlete isn't taking it year round. He might take it for a couple of months, and get the gains he needs or she needs, and then stops it and goes on to a conventional anabolic drug. So they're not staying on it year round. Now I'm sure there are some people who might.

Mr. SIKORSKI. Once they use it, isn't there a reversion, or isn't there——

Mr. KERR. Alas, the gains remain rather nicely.

Ms. THOMPSON. I had heard 7 weeks, that you only needed to use it 5 to 7 weeks.

Mr. SIKORSKI. Thank you.

Mr. WAXMAN. Thank you, Mr. Sikorski.

We are going to have to break now because the Full Committee is ready for us to take up another bill.

I just want to ask one question of Dr. Voy. Have either Genentech or Eli Lilly Company contacted you or the Olympic Committee concerning any interest in assisting in the development of a means of testing for illicit use of human growth hormone?

Mr. VOY. No. We don't have any connection with a pharmaceutical company. As you know, we operate on contributed funds and sponsorships. We'd love to have a pharmaceutical company as a sponsor, because there's a great deal of money there, but for this very reason, not just growth hormone, but the other drugs of abuse, we are reluctant to take on a sponsorship of a pharmaceutical company.

Mr. WAXMAN. For a minute I thought you were asking for one.

Mr. VOY. Oh, we'd love to be able to do it if it weren't going to be a misperception of what our object was.

Mr. WAXMAN. We are going to break now. We will reconvene at 1 o'clock, rather than 2 o'clock, and we will meet in room 2123, which is on the first floor of this building.

We thank the witnesses on this first panel. I don't think there is any necessity for you to come back. We appreciate your testimony. It's been very, very helpful to us.

Thank you.

AFTER RECESS

Mr. WAXMAN. The meeting of the subcommittee will come back to order. I apologize to our guests that we were delayed in reconvening this hearing, due to the time taken by the Full Committee.

Our next witnesses represent two drug companies involved in the manufacture of human growth hormone.

James Gower is the Vice President for Marketing for the Genentech Company of San Francisco. In October 1985, the Food and Drug Administration announced approval of Protropin, the first biosynthetic product found effective in treating children with growth hormone deficiency.

Leigh Thompson is a physician and vice president for Clinical Investigation and Regulatory Affairs of the Eli Lilly Pharmaceutical Company. Just last week, the FDA approved marketing of a new human growth hormone product. The availability of this product is currently the subject of litigation.

I want to ask Mr. Gower and Mr. Thompson to please come forward.

We are pleased to welcome you to our subcommittee hearing. We have your prepared statements. They will be made part of the record in full. We'd like to ask, if you would, to summarize in no more than 5 minutes.

Mr. Gower, we will start with you, and I think there's a button on the base of the mike that you have to push to turn it on.

STATEMENTS OF JAMES M. GOWER, VICE PRESIDENT FOR MARKETING, GENENTECH, INC.; AND W. LEIGH THOMPSON, VICE PRESIDENT, CLINICAL INVESTIGATION AND REGULATORY AFFAIRS, LILLY RESEARCH, ELI LILLY AND CO.

Mr. GOWER. Thank you, Mr. Chairman.

Genentech certainly stands ready to assist this committee in any way possible in placing any appropriate restrictions on the prescribing of growth hormone that would lead to a reduction and the therapeutic misuse of the product.

We don't feel that DEA scheduling is particularly appropriate, however, because we don't really think, to be quite honest, that it will change anything in terms of what you've heard this morning, since there is a system primarily in place to provide auditability of the physical distribution of the drug, which is—we heard about some cases of diversion and some bogus products this morning.

We have, because we didn't feel that this was appropriate at the time of marketing, put some things into place already that we feel are actually already more restrictive than DEA Schedule II and perhaps more importantly don't involve either economic or implementation burdens on the parents of the children who the FDA approved this hormone for the use of.

And if I could, I would just briefly like, without being redundant and with the written testimony I gave you, to highlight the key elements of that system, because I think it's important to illustrate a real live situation in terms of the children who legitimately need this hormone, as opposed to athletes or others who would simply like to have it.

Specifically what we have done is to put in place a system that has two distribution channels. One utilizes a home health care firm by the name of Caremark located in Southern California. The other is to select hospital pharmacies, and those are, without exception, either major teaching centers or children's hospitals, where we have requested that the hospital pharmacist place growth hormone on a restricted formulary. What restricted formulary means is that it would not be available ordinarily to all physicians on staff, but to those that are agreed by the Pharmaceutical and Therapeutic Committee are appropriate prescribers of this growth hormone.

Almost every pharmacy has complied with this request, and right now I think it is accurate to state that of the growth hormone being distributed from our company, Protropin, we cannot only physically verify the distribution of 100 percent of the growth hormone, which is what is required by DEA scheduling, but in a rather unprecedented move in the pharmaceutical industry, because we were worried about the potential for misuse of this product from the very beginning.

We can physically verify the appropriate prescription, including such things as the basis for diagnosis and the physician's name, through either our post-market surveillance study or through the records we have access to at Caremark, which are blinded only as to patient confidentiality, on over 70 percent of the children being treated. That is really an unprecedented number and something that DEA schedules really wouldn't add to.

Really, my last point, so as to not take too much of your time, is to tell you what DEA scheduling would do, which we think is detrimental.

DEA Schedule II prohibits refill prescriptions, telephone verification of prescriptions except in cases of an emergency, and indirectly limits the size of the prescription that can be filled in almost all cases, since it's designed for psychoactive substances which are primarily acute use situations, as opposed to chronic use substances like growth hormone or human insulin or others that are used for many years in chronic therapy.

What this pragmatically does for a child is that it means in order to have easy access to growth hormone under Schedule 2, he must go back and make medically unnecessary visits to the physician to get the prescription rewritten, because that's what the regulations require. In many cases and in the case of a child that lived at some distance from the medical center where he was being treated, based on some insurance reimburse schemes that require less than a month's prescription, it could mean as many as 24 trips a year just to simply obtain the prescription, come back and obtain the drug.

We feel that would add certainly a lot of burden and potentially a lot of cost to the child in terms of obtaining the growth hormone.

As a last point, the case can be made that DEA Schedule II—and this is what frightens me the most—could be relied on by others coming into this marketplace as being the primary protection, because it sounds good. And quite frankly, I feel that any sports medicine physician out there who has a license to practice and DEA schedule number—and they all do, because they have to prescribe Empirin with Codeine and other sorts of painkillers, can have easier access if that schedule is relied on instead of some sort of control not on the physical distribution, but control on who is able to prescribe and who is not.

The FDA and the DEA can't force us to put in place these sort of controls, but we voluntarily put them in place because we're worried about the very same problem.

So we stand willing to help you on things that would help control abuse without putting unnecessary burden on the children, and I would like to start with, if I could ask your assistance in obtaining the lot number of the Protropin that Dr. Kerr said he obtained this morning, we would like to find out where that came from.

[Mr. Gower's prepared statement follows:]

STATEMENT OF JAMES M. GOWER

Mr. Chairman and members of the Committee, I am James M. Gower, Vice President of Marketing at Genentech, Inc. Genentech is a leading biotechnology company committed to the research, development, and commercialization of pharmaceutical products made through recombinant DNA techniques. Since 1976 we have been involved in the research and development of a number of important pharmaceuticals that would not be possible without the new tools of biotechnology. Among the recombinant pharmaceutical products which we developed and for which we have received FDA marketing approval, are human insulin for diabetics, alpha interferon for patients afflicted with a certain type of cancer, and human growth hormone for the treatment of growth disorders in children whose bodies cannot make adequate levels of growth hormone. We have a number of other exciting and promising products in the pipeline, such as one which dissolves clots in heart attack victims, called tissue plasminogen activator, which we asked the Food and Drug Administration (FDA) to license in April, 1986.

To date, however, the only product which we have developed and brought to market in our 11 years of corporate existence is Protropin® (somatrem for injection), the trade name for our recombinant human growth hormone. We market Protropin in the United States and Canada. Kabivitrum, a Swedish company owned by an agency of the Swedish government (to which we have licensed our technology for producing Protropin) distributes our human growth hormone product outside the United States and Canada.

Since the early days in our development of Protropin we have been aware of the potential for misuse of the product. Prior to the commercialization of Protropin, Genentech consulted extensively with the American Academy of Pediatrics and the Lawson Wilkins Pediatric Endocrine Society. Our mutual goals were to develop a distribution and control system that would address the potential for growth hormone's misuse without imposing unnecessary burdens on the families of children who need this drug to correct an endocrine system imbalance which prevents their growth and maturation. We at Genentech believe that we have done a good job in meeting these two goals.

Our view of the potential misuse of Protropin and other human growth hormone products is that the drug may be desired by athletes or parents of children who would like to have their children grow taller. At the root of this potential for misuse is a physician who is willing to misprescribe the drug. We are concerned with potential misuse and would support legislative restrictions which are aimed at limiting the prescription of Protropin for inappropriate uses.

I would like to share with the Committee the details of our system for distributing Protropin. It is a system far more restrictive than that which could legally be imposed on us by the FDA or the Drug Enforcement Administration (DEA). At our system's core is a limitation on the types of physicians who can prescribe Protropin in order to avoid any misprescription. Thus, we distribute the drug only to designated distribution centers in order to assure that access to Protropin is limited to appropriate medical specialists: pediatric endocrinologists and other endocrinologists. We also verify through post marketing surveillance, that these physicians have diagnosed properly growth hormone inadequacy.

Specifically, Genentech distributes Protropin only through Caremark-Home Health Care of America and designated hospital pharmacies. We have no financial interest in either Caremark or any of the hospital pharmacies that distribute Protropin.

We use Caremark, a home health care company, as a primary distributor because it is convenient for patients and because it provides additional safeguards to insure that Protropin is used only to treat patients who have been properly diagnosed as growth hormone deficient. In addition to a prescription, Caremark requires a statement of medical necessity, including a diagnosis signed by an appropriate medical specialist for each patient, with supporting details of the diagnosis, before the drug is dispensed.

The only other means by which Protropin is made available through distribution is to select hospital pharmacies in major medical centers. Recognizing that even this limitation poses some potential for therapeutic misuse of Protropin, we request dispensing hospitals to place Protropin in restricted formularies so that only certain physicians authorized by the hospital can prescribe it.

We believe that Genentech's closed distribution system is effective and that additional controls on the distribution of Protropin are unnecessary. We already track closely the Protropin we distribute through our two distribution channels and routinely check for any suspicious use or diversion. Thus, placing human growth hormone on any DEA schedule would simply add to the paperwork, but not to the effectiveness of our system. More importantly, between the records to which we have access at Caremark-Home Health Care of America and the data we hold directly on the over 1,700 children that we follow in our post-market surveillance study, we can identify and audit almost 70 percent of all the patients for whom Protropin is prescribed. Our data base for these patients includes: diagnosis, patient age, dose of growth hormone, frequency, and the prescribing physician. In other words, we are able not only to verify the physical distribution of Protropin, the focus of DEA scheduling; but in almost 70 percent of patients we can also verify the appropriateness of the prescription. We believe that this system is unprecedented in the pharmaceutical industry. We further believe that placing growth hormone on a DEA schedule would add nothing to the safeguards built into Genentech's distribution system.

The DEA scheduling system is focused primarily on assuring proper controls on the physical distribution of psychoactive drugs. The DEA system is not well-suited for monitoring the proper prescribing of scheduled drugs by physicians. In fact, to quote from a portion of DEA regulations applicable to scheduling, "The responsibility for the proper prescribing and dispensing of the controlled substance is upon the prescriber" (21 CFR, Section 1306.04). Specifically, if human growth hormone were placed on DEA Schedule II, any sports medicine physician in the United States would be able to prescribe growth hormone as long as he or she is licensed to practice medicine and is in possession of a DEA prescriber number (something all practicing sports medicine physicians have). Currently, these physicians do not have easy access to prescribing opportunities for Protropin.

Genentech opposes the placement of human growth hormone on the DEA schedule not because of any fear of lost revenues, but because we already have a more stringent distribution system in place. We oppose the scheduling of human growth hormone because it would make obtaining the drug more inconvenient and more costly for the very patients for whose benefit the FDA approved it.

Placing human growth hormone on the DEA schedule would prohibit prescription refills and prescription verification by telephone except in emergencies, and indirectly would limit the prescription amount that could be dispensed by a registered pharmacist to a growth hormone deficient child. These prohibitions would place unnecessary burdens on the families of these children. Since growth hormone is prescribed for a chronic condition, it is currently dispensed on a routine basis between scheduled physician visits. DEA scheduling would require families to revisit the prescribing physicians simply to obtain a new prescription; in some cases this would involve three to four times more visits than are medically required. Because treatment of growth hormone deficiency may extend over a 5 to 7 year period (or even longer), expenses for additional physician visits would be substantial. Where third party reimbursement requirements limit prescriptions to less than a one-month period, as many as 24 trips a year could be required.

Currently prescriptions for growth hormone are refilled by hospital pharmacies or Caremark, often by phone verification to the physician. Refills, however, of a Schedule II drug are prohibited by statute and DEA regulations require partially filled prescriptions to be completely filled within 72 hours. Therefore, for many families who live some distance from the medical center where the prescriber practices, additional and medically unnecessary trips would add significant cost as well as inconvenience to their lives. This inconvenience and cost, which would not provide additional effective safeguards, could result in parents asking physicians without appropriate training to prescribe growth hormone for their children.

With other growth hormone products now entering the market, DEA scheduling could actually have a detrimental effect on the control of growth hormone usage. Other manufacturers may simply rely only on Schedule II controls as a means of limiting distribution and refuse to use the self-imposed distribution controls that Genentech has pioneered. If that happens, other manufacturers' products may be more readily available at local pharmacies; this could force Genentech to consider alternative means of distribution in order to remain competitive.

In summary, Genentech opposes the placement of human growth hormone on DEA Schedule II for one fundamental reason—it will have a negative impact *only* on those who legitimately need the drug. We currently have in place a system that we believe is enormously successful in limiting access to growth hormone to those who use it properly. We stand willing to work with this committee to design additional controls on human growth hormone if they can be shown to benefit the public health and not present unnecessary additional burdens to patients and their families.

Mr. Chairman, I will be pleased to answer any questions you or other members of the committee may have.

Mr. WAXMAN. Thank you very much.

Dr. Thompson.

STATEMENT OF W. LEIGH THOMPSON

Mr. THOMPSON. Thank you, Mr. Chairman.

I am here today with Mr. John Holt, who is the Secretary and General Counsel of the Pharmaceutical Division of Lilly. I would like to try to summarize our statement in five points, based largely on the testimony you heard this morning.

First of all, the question is, will growth hormone have a beneficial effect on athletic performance? And I believe that there is no evidence that it will, and that there is evidence that it may be harmful.

Now there are two lines of evidence. First of all, this morning we heard anecdotal reports of the use of growth hormone, some of which may be only water in the vial, together with anabolic steroids, together with eating as many calories as possible—very difficult to make out what growth hormone might be doing to the athlete in that regard. Furthermore, the limited amount of growth hormone that's available make it very unlikely that any number of athletes have obtained in large amounts for a long period of time. The dose, of course, is related to body mass, and I doubt seriously that many athletes have received enough to have any effect from the growth hormone.

Now the second point is, I'd like to agree with Dr. Voy on what he said this morning about our knowledge about an excess of growth hormone. The condition of acromegaly is well-known, and as he pointed out, this leads to a large jaw, fingers, ears, feet, but it leads to muscle weakness. There actually is a disorder of muscle and also a disorder of nerves.

And our experience with acromegaly would suggest to me that an excess of growth hormone is not only not beneficial, but probably harmful in patients. I think if the athletes knew what we know about growth hormone, they would not be interested in misusing it.

Now the second thing is, will education work? We heard some debate about that this morning, but I think the athletes who testified are eloquent examples of effectiveness of education. They themselves were educated and stopped misusing drugs, and they are effectively educating other athletes in the proper approach to athletics and not misusing drugs.

I don't think that Dr. Voy meant to fully equate educational efforts of the USOC with punitive drug analysis. In fact, the USOC is working on educational programs, and of course the drug industry, like Lilly, is vitally interested in educating the profession and the public in the proper use of drugs. We know what our drugs will do when they're correctly used. We do not want them damaged by misuse in any way.

In addition, Dr. Voy suggested that the USOC had difficulty in accepting contributions from the pharmaceutical industry. But I want to point out that Lilly has quite a track record of aiding amateur athletics. Two years ago, we gave $235,710 to the University of Indiana to establish a drug analysis laboratory for amateur athletics, and that will be the primary lab in the Pan Am Games, and in addition, the company made non-commercial contribution of $1 million in support of those Pan Am Games.

Lilly is an expert in education about drug effects, and we believe that we would like to work with the USOC, the American College of Sports Medicine, and other bodies in educating athletes in the pharmacology of growth hormone to dissuade them from its misuse.

Now third, this morning Dr. Todd emphasized that the misuse of anabolic steroids has quite effectively been decreased by the current efforts, and I remind you that anabolic steroids are not subject to the Controlled Substances Act, and therefore the current system, at least in the regard to anabolic steroids, as he testified, is working.

Would the Controlled Substances Act work? Well, as Chairman Waxman noted this morning, that Act is largely for drugs that produce dependency, and I'm not aware that growth hormone produces either psychological or pharmacological dependency in the scientific definition.

Now finally, we do believe that there are two alternatives to the Controlled Substances Act that clearly will work. One of these is education, which I mentioned before, and the second is controlled distribution.

We just heard of Genentech's program of controlled distribution. Lilly also is shipping directly from Indianapolis to pharmacies where there is a specific need. We already have one example where a pharmacy requested the drug without a demonstrated need, and it wasn't shipped. We believe that we can control access in that fashion.

Now perhaps the best way to summarize is to quote from this morning's Wall Street Journal and the article by Alan Otten. In the last paragraph, he quotes Dr. Robert Blizzard, who was one of my professors and who is one of the leaders in pediatric endocrinology and growth disorders:

"The paperwork burden is bound to result in additional cost to the patient, says Robert Blizzard, Director of the University of Virginia's Children's Medical Center. Education and tight controls by the manufacturers should be the mechanism to prevent abuse."

I believe we agree with Dr. Blizzard.

Thank you.

[The prepared statement of Mr. Thompson follows:]

Statement of Eli Lilly and Company

Mr. Chairman and members of the Subcommittee, I am Dr. W. Leigh Thompson, M.D., Ph.D., F.A.C.P., a Vice president of the Lilly Research Laboratories. With me today is Mr. John M. Holt, Secretary and General Counsel of the Pharmaceutical Division.

It is a pleasure to provide these comments on human growth hormone.

Eli Lilly and Company has been involved in the research, development, production and distribution of human pharmaceutical products for over 110 years. At the present time, the Company has a significant commitment to innovation in biotechnology. These comments will address:

1. Growth hormones and their use by athletes.
2. The use and distribution of the Company's most recently approved product, HUMATROPE®—human growth hormone; and
3. Public policy considerations relative to the control of human growth hormone and comparable substances.

GROWTH HORMONES

There are numerous hormones that contribute to growth. These remarks will focus on one of these, human growth hormone, that is available as HUMATROPE® (somatropin [rDNA origin] for injection, Lilly).

Human growth hormone drug products are intended to permit normal growth in children who have been medically determined to be severely deficient in this substance. For about three decades the hormone derived from cadavers was distributed by the National Institutes of Health for treatment of thousands of children with growth defects. Despite such widespread use and distribution, little if any of the material was known to be misused.

Serious consequences can result from excessive amounts of this hormone. These consequences can be judged from the condition of acromegaly, caused when a pituitary tumor secretes more hormone than usual in adults. The jaw, hands, and feet grow larger, the patient may develop diabetes mellitus and hypertension, and there is generally muscle weakness. This muscle weakness is caused both by damage to nerves and by a disorder of muscle. In addition to weakness of skeletal muscle, the heart muscle may also be weakened; and heart failure is a common cause of death in patients with acromegaly.

MISUSE OF DRUGS AND NATURAL HORMONES BY ATHLETES

An often-mentioned potential misuse of human growth hormone is to improve athletic performance. The extent of misuse of growth hormones by athletes is not clear from anecdotal reports. In fact, there have not been adequate and well-controlled trials of the effects of human growth hormone on athletic performance, and observations of patients known to have extra amounts of human growth hormone do not suggest any beneficial effects on athletic performance. More importantly, the fundamental tenet of athletics is a quest for excellence—the achieving of a "personal best." Misuse of drugs or natural hormones is cheating, and thereby may reflect disordered priorities and ethics of some athletes and organizations that promote athletics.

Our efforts should be directed to achieving health and athletic goals in programs that are guided by health professionals and that discourage misuse of drugs, vitamins, foods, and natural hormones.

HUMATROPE—LIMITED DISTRIBUTION AND USE

Under routine conditions, Eli Lilly and Company distributes human pharmaceuticals through approximately 300 independent pharmaceutical wholesale distributors. HUMATROPE, however, which has been in distribution only since March 30 of this year, is distributed directly by "third party shipment" from Eli Lilly and Company in Indianapolis primarily to clinics and hospitals (Although the billings for such shipments are through and for the account of Lilly's authorized wholesale distributors, the HUMATROPE product itself is distributed directly to the clinic or hospital.) This is because the Company anticipates a very narrow range of market interest in HUMATROPE for its approved use, which is the treatment of pituitary growth deficiencies in children. There are now only about 5,000 patients with diagnosed growth hormone deficiencies in the United States. Most of these patients are treated by approximately 300 pediatric endocrinologists. Lilly's marketing efforts are directed to this limited group of specialists.

REGULATION OF HEALTHCARE

The Food and Drug Administration has the responsibility to approve drugs determined to be safe and effective for their labeled indications. Licensed physicians prescribe and registered pharmacists dispense such approved products. Lilly facilitates the proper use of its pharmaceutical products by extensive educational efforts. The utility of pharmaceuticals to society is best preserved by providing to our health professionals the best possible information as to the intricacies of health care.

THE SCHEDULING OF HGH IS INAPPROPRIATE UNDER THE CONTROLLED SUBSTANCES ACT

Lilly has had extensive experience with the Controlled substances Act. It produces and distributes pharmaceutical products in Schedules II through V. The Company supported the adoption of the Single Convention on Narcotics, 1961, and the passage of the Controlled Substances Act of 1970. It also has supported the scheduling of specific drugs that it has developed.

During the 99th Congress, the Subcommittee received for consideration H.R. 5653 and H.R. 5695, measures which would have amended Schedule II, Section 202, of the Controlled Substances Act by the inclusion of "somatrem and any other artificially produced growth hormone."

The Company understands that the Subcommittee may consider such legislation during the 100th Congress. In our view, the inclusion of HGH in Schedule II is inappropriate for the following reasons.

Present national and international controls represent efforts to limit the availability of substances which have hallucinogenic, depressant, stimulant and dependence-producing pharmacologic characteristics. Somatrem and other artificially produced growth hormones do not have these pharmacologic characteristics, and thus do not present the problem to which the Controlled Substances Act is addressed.

Moreover, to schedule "growth hormones" under the Controlled Substances Act would defeat one of the Act's most important advantages. As it now stands, the Act has provided certainty with respect to commercially-distributed controlled substances so that wholesalers, physicians and pharmacists can identify them. The drugs that are subject to the Act are specifically identified in the statute itself or have been added to the appropriate schedule by Drug Enforcement Administration regulation after considering the recommendations of the Food and Drug Administration. Controlled substances are identified as such in their labeling. This identification permits community and hospital pharmacists and licensed practitioners to maintain the necessary records to take inventories and to dispense and prescribe in accordance with the prescription limitations specified by the Act. The proposed inclusion of "other artificially produced growth hormone(s)" in Schedule II could result in the control of a wide range of agents not identified with certainty. This would frustrate those attempting to legitimately maintain records and controls of the distribution of ethical pharmaceuticals as well as those involved in law enforcement.

The Controlled Substances Act is a carefully balanced scheme for dealing with the distinctive and multifaceted societal problems presented by the non-medical use of dependence-producing dangerous drugs, some having no legitimate medical use whatsoever. The Act was never designed for dealing with issues that might be thought to arise from medical use of legitimate pharmaceuticals for diseases or conditions beyond those reflected in the drug's labeling. The possibility that human growth hormone products might be prescribed for such additional diseases or conditions, if it even exists to any significant extent, has nothing to do with the issues of drug dependency and nonmedical abuse that the Controlled Substances Act addresses. If certain types of drugs are to be subject to mandatory restricted distribution and use arrangements, such proposals should be carefully thought out. Criteria for inclusion of drugs under such plans should be established with information obtained from all appropriate sources.

We urge the Subcommittee to secure the views of the American Medical Association, the Pharmaceutical Manufacturers Association, and the American College of Sports Medicine. other health professionals in pharmacy should also be consulted, as should the Department of Health and Human Services and the Drug Enforcement Administration. These organizations may assist the committee in efforts to quantify the incidence of asserted misuse of human growth hormone and to develop necessary recommendations.

In any event, Eli Lilly and Company urges that to add "somatrem and other artificially produced growth hormone(s)" to Schedule II would be both unjustified and unwise.

We would be glad to respond to questions from the Chairman and members of the Subcommittee.

Mr. WAXMAN. Thank you very much.

Mr. Gower, let me ask you about the deterrence value of Schedule II. I've heard that a shipment of Protropin was stolen from a Caremark location. Are you familiar with the details of that incident?

Mr. GOWER. Yes; I am.

Mr. WAXMAN. I understand the Protropin was clearly the target of the thieves, since they went to two different sites. This certainly seems to confirm the value of the drug on the black market. What I'm interested in is that the thieves specifically bypassed a quantity of morphine, a Schedule II substance, but stole the Protropin.

What are the penalties for trafficking in Protropin compared to those of trafficking in morphine?

Mr. GOWER. I can respond in two parts. First as to the facts of the issue and we are still corroborating with the Department of Justice and their task force in investigating this incident. I think that example is one of the best examples of why Schedule II won't help. The reason that the morphine you mentioned was left there—morphine was left there, and morphine of course is a Schedule II drug. That drug was stolen from a locked controlled area for Schedule II drugs, precisely what is required by the Act and it didn't stop the thieves from doing anything, in terms of coming in and stealing 662 vials.

To date, the only diversion that we know of and in asking the Department of Justice last week, the only one they know of. They have found exactly four vials of Protropin and their wide range of investigation is finding hundreds and thousands of vials of steroids out there.

We think the system although not perfect is working.

Mr. WAXMAN. Isn't it the case that if they had taken that morphine, they could be subject to 15 years for trafficking in morphine and for taking the Protropin, they may get a 1 year penalty of imprisonment.

Do you believe that the current controls under the Food, Drug and Cosmetic Act combined with your voluntary controls are sufficient to deter such crimes and punish violators?

Mr. **Gower**. Yes, sir, I do, in the face of testimony this morning. If Dr. Todd is to be taken literally, that athletes would be willing to risk death, then to me, 1 year versus 15 years, any prison time would frighten the daylights out of me but the difference in the statutory requirements for time served wouldn't seem to be much of a help in terms of an effective deterrent and it would be much simpler just to add that on to existing food and drug acts, if that is important.

Mr. **Waxman**. Make it the same period of time?

Mr. **Gower**. Sure.

Mr. **Waxman**. That's one possibility, but obviously if they are going to be faced with a crime that is going to mean a 15 year sentence, they may think about it and be a little more concerned about it. It is a stiffer penalty than a fine or 1 year in jail.

Could you supply a list of lot numbers involved in the instances of this Protropin discussion? We would like that for the record.

Mr. **Gower**. We would be happy to. I think Dr. Budetti has already received such a list. I'll make sure that you get everything we have.

Mr. **Waxman**. In approving human growth hormone, the FDA was careful to limit the indications for its use to growth hormone deficiency. Why did the FDA find it necessary to impose this limit?

Mr. **Gower**. Well, sir, that's the only thing that it has proven efficacious for, ordinary policy.

Mr. **Waxman**. Your company, Genentech, quite candidly, recognized the potential for misuse of human growth hormone and I commend you for that. I agree with you that your distribution system is probably unprecedented in the industry.

I do not agree with you, however, that Schedule II would necessarily involve problems such as prohibiting refills and telephone prescriptions, since we would certainly amend the statute to accommodate the usual treatment schedule for children who need the drug. Let's leave aside our disagreement over Schedule II for a moment.

I'd like to follow up with you on your statement of support for legislative restrictions which are aimed at limiting the prescription of human growth hormone for inappropriate uses. What would you consider an inappropriate use? How would that be defined, other than the ones approved by FDA or in some other way?

Mr. **Gower**. I would certainly think that the easiest place to start is for the approved indications being the limit of the use. That has certainly been applied as a standard by the Compliance Division of the FDA over a number of years and seems to work pretty well. I think that is a pretty good place to start.

Mr. **Waxman**. American medicine and the pharmaceutical industry have traditionally opposed those kind of use restrictions. Do you think your proposal would have any serious chance of being enacted?

Mr. **Gower**. Sir, you are asking me to have an opinion in an area that I'm not qualified to answer.

Mr. **Waxman**. I assume you would know the pharmaceutical industry and their historic opposition to this kind of use restrictions. Do you think they would oppose it?

Mr. **Gower**. I think if it was made growth hormone specific, if you wish, there are certainly a number of pediatricians and pediatric endocrinologists that would like to see this drug controlled in terms of its usage and I think the chances might be quite good. They certainly want to keep it out of the hands of sports medicine physicians. That goes without question.

Mr. **Waxman**. Dr. Thompson, you say that Lilly recommends that its pharmaceutical products be used in accordance with the approved labeling. What do you think of Genentech's proposal for legislative use restrictions? Would Lilly support such an approach?

Mr. **Thompson**. I don't believe there is any evidence that the humatrope, which we just introduced a little over a week ago, is being misused outside of the label. This is a very special circumstance. There are only about 300 pediatric endocrinologists who care for children with hypopituitary growth deficiency and therefore, we have focused all of our efforts in terms of educating the physicians to the use of this drug to that small population of physicians. There are only about 5,000 patients who are being treated for that condition.

This is not the usual circumstance where the drug may be used by 400,000 physicians and a large number of patients.

Mr. **Waxman**. Notwithstanding that, you wouldn't agree with their idea of Federal legislation with that kind of restriction?

Mr. **Thompson**. I think such legislation would have to be considered very carefully because of its implications on other drugs.

Mr. **Waxman**. You are not endorsing it, you would want to see what other implications there are for other drugs. Do you think the rest of the pharmaceutical industry would be as cautious about that proposal as well?

Mr. **Thompson**. I can't speak for the pharmaceutical industry but any legislation obviously deserves careful study.

Mr. **Waxman**. I believe that. What are your thoughts on Dr. Sodeman's suggestion that an inert marker be placed on synthetic human growth hormone to permit testing that would aid in identifying human growth hormone abuse by young athletes?

Mr. **Thompson**. Such inert markers have been used in clinical trials in the past, to check whether or not the patient is actually taking the drugs. For example, one of the most commonly used is riboflavin, a common vitamin, which can be detected easily. That certainly could be attempted. I think we would be asked by the Food and Drug Administration to demonstrate the safety and efficacy, both of the inert ingredient and the combination. There is always the possibility for some drug/drug interaction or some idiosyncratic reaction to whatever you added.

Although I think that deserves some study, I do not believe there is a precedent for the addition of such markers in any currently marketed drug.

Mr. **Gower**. May I comment?

Mr. **Waxman**. Yes.

Mr. **Gower**. I was a little surprised by Dr. Voy's statement this morning that testing couldn't be applied in terms of growth hormones and it wasn't fitting with my knowledge of what I understood from my scientists. I called back just to make sure, since I am not a scientist.

I was told there is now in the literature and in routine use at Genentech, both blood and urinalysis for both growth hormone and somatomedin which is the downstream biochemical that is produced by the liver, and that indeed, at least according to what I was told today, and I will be glad to share that with Dr. Voy and anyone else, ought not to necessitate a marker, if there are indeed test procedures that can be used to track it already.

Mr. WAXMAN. We will have to find out more information about that. Thank you. Mr. Coats.

Mr. COATS. Thank you, Mr. Chairman.

Dr. Thompson, explain to me again your control procedure. You are only marketing or distributing to 300 endocrinologists?

Mr. THOMPSON. That's right. That is the target population of our educational and detailing efforts. When a pharmacy wishes to supply a growth hormone, that is shipped directly from Indianapolis. That would allow us to detect any unusual use by a single pharmacy. Because we know these pediatric endocrinologists and where the patients are located, it is unlikely that any substantial amount of growth hormone could be diverted from that controlled distribution system.

Mr. COATS. You are matching, if you receive a request from a particular pharmacy, you are matching that with your knowledge or records of an endocrinologist in that area that might be treating and prescribing?

Mr. THOMPSON. That's correct, Mr. Coats. It is largely done through the sales force who of course know the physician population and the pharmacies as well. We already have one specific example where a pharmacy requested a supply of the material and we couldn't identify a legitimate use and refused to ship it. We certainly intend to continue that policy.

Mr. COATS. Tell me a little bit about the detrimental side effects of use of this drug. There seems to be the impression left this morning that athletes—the word was out that occasional injections, a 7-week injection period is enough to promote the kind of muscle growth the athletes were looking for.

How correct is this? What kind of things should we be looking at, if we are going to spread educational information about this? What are the facts here?

Mr. THOMPSON. I think there are two possibilities. First of all, short term use of small doses as described this morning probably would not have much in the way of measurable effects. The second thing is——

Mr. COATS. Those athletes are getting measurable effects. You are suggesting that is coming because they are doing it in combination with steroids and a number of other things?

Mr. THOMPSON. Psychological effect. After all, a large amount of athletic competition is psychological rather than physical. I do think, however, as Dr. Voy emphasized, although we don't have good studies of the administration of this drug to athletes, the natural disease, acromegaly, provides us with a model of an excess of growth hormone in adults. We know those people are not star athletes. They are not the winners in athletic games. They are actually weak. Drawing from that, I would conclude that we don't have scientific evidence that it would help athletes and in addition, we do have scientific evidence that excesses would be deleterious.

In a statement of pediatric endocrinologists recently, they estimated that some of the effects of acromegaly were seen with as little as twice the normal amount of hormone. We are not talking about huge doses producing those.

Mr. COATS. You are saying that an athlete that obtains the growth hormone, even if they are injecting it on a less than regular basis, could be in a sense oversupplying growth hormone to their system and subjecting themselves to risk of some pretty disastrous side effects?

Mr. THOMPSON. I think the harm would clearly out do any hint of benefit and that if they knew of the consequences of excessive amounts of growth hormone, they certainly would not try to obtain it and use it.

Mr. COATS. How can we get this information out into the weight clinics, the training camps, into the system, about the risks of this thing?

Mr. THOMPSON. I think the pharmaceutical industry working together with organizations, with vital interests in sports medicine, such as the American College of Sports Medicine, the Olympic Committee and so forth, can easily provide this information to the athletes.

Mr. COATS. What are you doing to do that?

Mr. THOMPSON. We are mounting a major educational campaign with growth hormone that has been directed primarily towards the hypopituitary children with growth defects. Obviously, we have a large track record of educating the public with drugs such as insulin, for example, which is an over the counter product. We worked with the American Diabetes Association and other organizations to make sure that diabetic lay people know about that drug and the consequences of diabetes.

Mr. COATS. Are you doing anything to get the information about the potential negative side effects into the hands of the trainers and the Olympics people, college coaches, all those people that are associating with the athletic side of the use of this drug?

Mr. THOMPSON. So far in the first 9 days of our marketing, we focused on the physicians and the parents and patients, the children who have the disorder. We certainly stand ready to work with other people in providing this information. We have the information.

Mr. COATS. Tell me about this drug testing facility that you helped fund for the Pan American games. Will that facility have the capability of testing for growth hormone and will they do that?

Mr. THOMPSON. The facility has a capability of measuring growth hormone, however, that would be difficult to do in athletes. As Dr. Voy I believe pointed out this morning, the drug does not immediately increase athletic performance. If one were using the drug and stopped a number of days before competing, I do not believe one would find measurably increased amounts of growth hormone.

The humatrope product that we make is exactly the same as a normal pituitary hormone.

I think that will be a difficult issue and that one would only be able to detect its misuse if one measured it shortly after the injection.

Mr. **Coats**. Dr. Gower, do you want to comment on that? You mentioned that you thought testing was a viable alternative.

Mr. **Gower**. First, let me clarify that I am not a doctor. What I said was our physicians and experts in this area when I called, just to clarify that point, felt that although Dr. Thompson is quite correct in terms of the short term ability to detect growth hormone, it can be detected in the urine, it doesn't require blood sampling, which was also one of Dr. Voy's points. Second, there is a downstream biochemical that hangs around a bit longer, which is called somatomedin.

Mr. **Coats**. How long does that hang around? Do you know?

Mr. **Gower**. The studies that I had quoted to me over the phone showed that in cases of prolonged use of the drug, it was detectable in a matter of some weeks later. It wouldn't be at long periods of time. I was quoting a study from Japan and one that's in publication or about to be published out of the University of New York.

Mr. **Coats**. Could either of you comment on what placing this growth hormone on a Schedule II basis would do to its price? What is involved from your standpoint and how does that affect the price?

Mr. **Gower**. From our standpoint, meaning the manufacturer, it wouldn't affect the price. However, where the impact on the children would be, would be from the passed on mark-ups at the pharmacy level, from the burden of having to keep a separate inventory and go through the very burdensome paperwork that is involved in a Schedule II drug.

I can't predict exactly what that would be. In the past, when drugs have been scheduled, albeit very different drugs than this and one would hope pharmacists would be responsible about this very expensive medication, there have been associated pass ons of the costs required to comply with Federal regulations on the part of the pharmacies.

Again, from the manufacturer's level, I wouldn't anticipate a price increase.

Mr. **Coats**. Of course, considering the volume, the low volume of the distribution of this drug, I wouldn't think that would be excessive, even at the pharmaceutical level. They are not making hundreds of entries a day.

Mr. **Gower**. I think on a drug this expensive, any percentage mark up would be excessive when applied to the family of the children that have to pay for it. That's really where I was focusing.

Mr. **Coats**. What is the current cost for a family for treatment of this, per month?

Mr. **Gower**. From our post-market surveillance study of almost 2,000 children, the average patient weight was about 25 kilograms, the average dose, about .07 milligrams per kilogram and at the average injection of three times a week, an acquisition cost based on distribution through Home Health Care of America, it would be just under $12,000 a year. It is very expensive.

Mr. **Coats**. If an athlete wanted to get on a viable program of prolonged injection of growth hormone for a period of time sufficient to really make a difference, how much is it going to cost him and how long does he have to be in the program?

Mr. **Thompson**. We don't know what the effects would be in athletes of giving them virtually any dose but remember that the dose is usually related to body mass and athletes have an average body mass of probably at least four times that of the children that you cited. Knowing the general pharmacology of the drug, I doubt that you would see very much effect in less than a period of months. I think it would be a significant cost barrier.

Mr. **Coats**. Several thousand dollars?

Mr. **Thompson**. Oh, yes.

Mr. **Coats**. Easily, several thousand dollars, which I assume would make it a little bit easier to trace, because they are having to procure the drug in pretty sufficient quantity. It is not just an occasional box of Protropin that somebody gets through the mail. That box that we had this morning, that dosage, how long would it take a 200 pound athlete?

Mr. **Gower**. It wouldn't be sufficient for a 200 pound athlete. It wouldn't even be one dose.

Mr. **Thompson**. If you want to look at approximately doubling the normal amount of growth hormone that is put out by your pituitary gland.

Mr. **Waxman**. Would the gentleman yield?

Mr. **Coats**. Yes.

Mr. **Waxman**. Isn't part of the problem that we don't really know what the impact is this drug will have on people who want to use it for purposes other than those for which it is intended? Because we don't know that, athletes will believe that it is going to do them some good. Isn't it also the case with steroids? Many people thought steroids didn't do anything good for athletes for many, many years, although the athletes believed it, and it turned out steroids did increase their athletic ability.

Isn't there a credibility problem? You are saying even without the sufficient knowledge to make this absolute statement, this won't do any good for athletes, for those athletes that look back at the steroid example and think that if something is going to make somebody taller, why wouldn't it be helpful for them to be more competitive, to take this.

Mr. **Thompson**. Mr. Chairman, we are in fact pursuing research on growth hormones to look at its metabolic effects on protein, on carbohydrate, on fat in the body, on bone metabolism in the body and so forth. We will learn a lot more about this hormone in the next couple of years, even if we don't have any research directed directly at athletic performance. And I think that information is important. More important in having the information in our hands or in medical journals is getting it in the hands of athletes. And that's why I emphasize the importance of educational campaigns.

Mr. **Waxman**. What can you tell them? You can tell them you haven't done the studies, so you don't know how effective it really is. You think there are some downsides to it, that there's a risk, and you may even want to tell them you don't think it will do them any good. But the problem is they may not believe you, and probably won't, because they were told that steroids wouldn't do them any good, either, and they are going to think therefore why not take it. It may do some good, why not, and the athlete would say to himself, I never believed all those stories about the side effects, because after all I am somewhat invincible anyway. I guess that's the problem that we may be facing.

Mr. **Gower**. Mr. Chairman.

Mr. **Waxman**. Yes, Mr. Gower.

Mr. **Gower**. I think you bring up a valid point. That's in essence what I was saying in terms of the—the misuse really is one of an athlete who, as we heard this morning, is driven to do some pretty irrational things in the quest for greater athletic performance. But at the core of specifically the DEA scheduling system is nothing that would change that and, more importantly, nothing that would change the ability of thefts and diversion aside, if I may, because I really think that's a separate issue. It would not deter a physician from prescribing for anything they wanted to. In fact, the section of the Federal regulations that relate to scheduling, and so you'd have to do quite a bit of surgery, quite honestly, state that the responsibility for proper prescribing and the dispensing of the controlled substance is upon the prescriber.

DEA makes no attempt to address that.

Mr. **Waxman**. I don't think our fear regarding athletes is what the doctors will prescribe. Our fear is that through this diversion area or chain, people can figure there's money to be made by diverting it, and they're going to get ahold of it, not because of doctors prescribing it, but because they're likely to feel that they can take the chance, since it's not 15 years in jail, that maybe they can get away with it, because they stand to make a lot of money.

Mr. **Gower**. You may have a very good point on the jail. I don't have an opinion on that. It sounds logical to me. But I think the point I was trying to make earlier, and the point that I believe the Lilly folks were saying as well is that the existing distribution systems in place are arguably, and I think convincingly, already more restrictive than that required by DEA scheduling in terms of——

Mr. **Waxman**. I don't see how you can say that when we already had an example this morning, and you haven't been marketing it for that long. Someone was able to pick up a whole boxful of this stuff very, very easily, even though you claim you have a control system in place that is effective. It obviously wasn't effective for that box, and I can't say it's more effective than Schedule II, because I think Schedule II holds out the hope of being as effective as it can be for these controlled substances.

Mr. **Gower**. I'm sorry to reiterate, but again in collaborating with the Department of Justice in their task force—excuse me, DEA and FDA and their task force on steroids and abuse in athletics versus the hundreds of thousands of vials, there have been exactly five vials of protoprin that they have uncovered. Their statements to me were it is very hard to get.

Mr. **Waxman**. Well, I thank you for your testimony. We will look forward to talking about this issue further while working with you to see what we can do about a problem we hope will not become more widespread. Thank you very much.

Our final witnesses this morning have been asked to appear representing parents of children suffering from growth disorders. Sheila Chadwick is from Reston, Virginia, and the parent of an 18-

year-old young man who has used growth hormone since 1978. Carl Coussan is a parent and public affairs coordinator of the Parents Council for Growth Normality. We welcome the two of you to our hearing today. We have your prepared statements. We would like to ask, if you would, to summarize in no more than 5 minutes.

Ms. Chadwick.

STATEMENTS OF SHEILA CHADWICK, RESTON, VA; AND STEPHEN CARL COUSSAN, PUBLIC AFFAIRS COORDINATOR, PARENT COUNCIL FOR GROWTH NORMALITY

Ms. **Chadwick**. I am Sheila Chadwick. Thank you for having me here, Congressman Waxman and Mr. Coats.

I have come with a picture so that we can personalize what it is we are talking about. May I bring this up to you?

The child in the gold colored jacket is my oldest son. At the time this picture was taken, he was 9 years old. I think that you would find it very difficult to recognize that you were looking at a 9 year old child in that gold jacket. He had not yet started on growth hormone treatment, and his bone age at that point in time was 4½ years of age.

For 5 years we had been very concerned about his obtaining treatment, because we knew he had some kind of growth disorder. All of the tests indicated that he had some circulating human growth hormone in his system. Consequently, by the rules that were then in regular use, he was unable to obtain human growth hormone for treatment because he did not qualify to get it. That was a regulated drug, administered by the National Hormone and Pituitary Agency.

For 5 years he also did not grow. About 2 weeks after the picture was taken, he was retested and this time, given the same set of tests, was found to have a total deficiency of circulating growth hormone, therefore qualified to take the drug, and was considered for research protocol.

Because of the scarcity of biological growth hormone, it was 8 months before he was able to obtain the start of treatment. So at that point he was 9½ years old.

Since 1978, and up until the drug was withdrawn from the market a year and a half ago, he was on biological growth hormone. Within 6 months of taking the drug, he did begin to grow and experienced internal maturation as well as external maturation.

My other picture was taken at the time he stopped taking the drug, and you will find that he is the youngster over here. He's still the oldest one of the crew. He's 5 foot 3 inches. The remaining children will all be about 6 foot 5 inches or taller, as their father and I are both quite tall.

If this legislation that has been proposed goes into effect, I think that it will affect a large number of parents that have been in the same boat that I have been in the 9 years or actually 18 years of attempting to obtain treatment for my son.

The DEA scheduling requires certain kind of recordkeeping, a certain amount of quota based on historical usage, and a certain requirement for visitation in order to have access to the drug. It has already been discussed before, what the visitation possibilities are, and what kinds of waivers might be involved. There is no question that if such waivers did not occur, that there would be an extraordinary expense to families to get in one case a family flying from Chicago to Charlottesville in order to pick up their child's Protropin. In another case a family from West Virginia going to Johns-Hopkins and so forth.

The treatment centers are widely scattered and the parents are all over the country.

Aside from the normal visitation schedule, we have stated and have heard stated any number of times that the requirement is that the child be hypopituitary. In the case of my son, as I indicated earlier, for 5 years he did not receive treatment because he was not regarded as hypopituitary. He clearly had a growth disorder, but nobody could say what it was and no one would give him a trial of the drug because biological growth hormone was in such incredibly short supply.

We would, with the quota system and very strict regulations for a child passing tests that indicate procedurally that he is hypopituitary, find ourselves in the same situation that I was in with my son, and many, many other parents—indeed, three quarters of the parents whose children currently take human growth hormone today are not parents of documented hypopituitary children. About one third of the children taking human growth hormone have hypopituitariasm subsequent to a brain tumor, but the remainder have various other causes in terms of why they have a child that doesn't grow, and most of those are not diagnosed.

So those children would all be liable, their physicians would be liable to criminal penalties under the DEA if they prescribe for those children on a trial basis.

In fact, my son at 15 again had human growth hormone circulating in his blood, and therefore was not able to obtain access to a particular research protocol we wanted him to go on.

We nevertheless continued him on human growth hormone for the next 2 years, and he did grow. He would not have grown without it.

I have indicated in my testimony that I have a suspicion that my son may need to have some kind of a maintenance dosage of human growth hormone. We have no knowledge whatsoever of what happens to the children who have been on human growth hormone after they reach maturity. There has been no research. We don't know what it does to athletes, because we don't have any research even on what it does to acknowledged type of pituitary individuals who have been on this drug before.

I really think that we have been talking about quackery in the morning, and what the side effects for society of quackery are. Instead, I do believe that we should be focusing on the group for whom this drug was developed. And if we do that, I think the logical answer is to initiate research, government-directed research, that would be a coordinated program that would reveal what this drug in fact does. And I have proposed in my testimony an advisory panel to that effect.

In that case, I think we would have the substance of an educational campaign that the other individuals have spoken about that might in fact make it ridiculous for the athlete to spend the $40,000 to $50,000 a year he would need for the equivalent treatment that a child currently has at say $20,000 a year for a teenager size in growing, using this drug.

I would also like to add that I do not have any ties to any drug companies, I have no investments. The only personal stake that I have is in this youngster and in the children of other parents with whom I have associated over the years in obtaining treatment.

[The prepared statement of Ms. Chadwick follows:]

STATEMENT OF SHEILA BRASS CHADWICK

Mr. Waxman and Honorable Representatives, My name is Sheila Chadwick. I live at 11204 Hunting Horn Lane, Reston, VA 22091. I am the mother of an 18 year old son who has used human growth hormone since 1978. I am offering testimony regarding the proposed legislation to place HGH on regulated Schedule II status according to the "Controlled Substances Act." My concerns are based upon my personal experience in obtaining treatment for my son, and a great deal of additional experience in the parent support group I initiated with pediatric endocrinologist Dr. Val Abbassi, MD., of Georgetown University, in 1980, through which group I have learned a great deal about the accessibility of treatment for various growth disorders and helped many other parents obtain guidance and treatment for their children's growth problems. I have no special ties or investments with any drug manufacturer, treatment center, or physicians' group. I speak only for myself, but many of the parents in my group echo the same concerns about this proposal that I have.

As a parent, my primary concern is obtaining treatment for my child. To this end, what is important to me is an accurate diagnosis, safe, efficacious, accessible and affordable treatment. It is essential that there be ongoing, coordinated research to uncover the complex interrelationships of the many different symptoms of growth disorders besides extreme short stature. It is my understanding that the purpose of this bill is to inhibit abuse of HGH. I am not sure if the bill would succeed in doing that, but I feel sure that it would harm the population that HGH was developed to help: children with growth disorders.

The regulations would require specific record keeping and dispensing documentation by physicians and pharmacists. This might deter unscrupulous dispensers out to make quick dollars on the HGH "fad" in which the drug is regarded as a panacea for weak muscles, flabby thighs and wrinkles as well as getting skinny six foot Johnny to 6' foot, 6 inches so he can play basketball. While such uses may be reprehensible in so far as there is currently little evidence that they work, and so would merely be costly quackery, nevertheless, they also pose no threat to the general public in the way mind-altering drugs and their related addictions do. Although the excessive dosage of HGH has the potential to harm, the likelihood of a user continuing a drug so costly as HGH with no beneficial effect seems extremely remote. Indeed, the steroid drugs which are not regulated, seem to be biologically much more dangerous, yet there is ample evidence throughout the world that they are overused and abused. I am concerned that increased and mandatory record keeping may exacerbate the costs without really curbing abuses. But I am more concerned that fear of a "record" of HGH prescriptions will deter legitimate physicians from appropriate trials of the drug with well-selected cases. I fear that the proposed bill is premature because so little is known about how HGH works. The history of advances in treating children with growth disorders has been through trial and error and fortuitous physician experiments.

When my son began his treatment with HGH, I had been trying for 5 years to obtain help with his obvious growth retardation. I began when he was 4 years old, at a prestigious University Hospital after my pediatrician observed my son's growth failure for more than a year. My son was subsequently given a complete test series; we were told that he had no underlying disease, did not lack HGH, and might be suffering from "maternal deprivation." In any event, there was nothing that could be done to help him. "Come back in 5 years if he is still having problems." At the time of the original tests he was a standard deviation below the bottom of the standard growth chart. We went to a psychiatrist, but still he did not grow.

At 8, when our son was again tested he failed each of the four tests of HGH activity; it was 8 months before treatment could be initiated because NHPA (National Hormone and Pituitary Agency) hormone was in such short supply. The gains were dramatic after he began to take HGH; not only did he begin to grow normally, but internal maturation took place as well; he gained fine muscle coordination as well as gross muscle improvement. Within 6 months of starting treatment, he could write legibly, kick a soccer ball and had a dry bed. But our physicians could not explain the mechanism by which this internal maturation occurred; they had not predicted these benefits would come along with improved growth velocity. My son was removed from the learning disabilities class in school and placed in the gifted/talented program.

Imagine how I felt when I could stop blaming myself for my beloved child's growth disorders, and help him achieve normality and competence at life's everyday tasks, as all his younger brothers could.

When he was 15½, I learned of a special research protocol that might delay puberty to enable him to have more years to grow, as he had "lost" much potential growth in the 5 years without treatment. In order to qualify, HGH deficiency tests were again done. This time however, he showed levels of circulating growth hormone greater than the permissible maximum for the study. The several endocrinologists involved discussed what the circulating HGH might mean. Was he now producing enough not to need HGH, or was his own HGH not "bioavailable" to him? No matter. He did not qualify for the study though we pointed out that his early childhood tests also showed HGH but the child dramatically failed to grow for 5 years, until HGH therapy was initiated. We elected to keep him on HGH therapy until epiphyseal closure, when long bones stop growing. Unfortunately that came all too soon with his active puberty.

Last June, at age 17, HGH therapy was discontinued. Since that time, it has become clear that there is a metabolic disturbance leading to incipient obesity that could be very dangerous to his health. Is the minute amount of HGH adults have circulating a mechanism of appetite control (homeostasis), the "appestat" the lay magazines describe in dieting articles? Last year he could bench-press a respectable weight, but this year he has perceptibly lost muscle tone. We think it is probable that although he is no longer growing taller, he may require a "maintenance dosage" of HGH, possibly throughout his lifetime, to mimic the normal HGH regulatory effect in normal people without growth disorder. Until the advent of biosynthetic growth hormone, such a therapy would be unthinkable because of the short supply for other equally needy dwarfed children. Now, the trial could be made thanks to the availability of a plentiful supply of HGH. But there is no precedent for prescribing HGH for the condition I have described in my son.

My point in recounting this history is that we simply do not know enough about growth disorders and HGH to limit the research physicians may be willing to undertake if they don't have to fear penalties. My child would benefit by such continued research. He certainly won't grow taller, and I am well aware of the potential side effects of overdosage, but obesity is itself a killer. Yet if HGH were regulated on Schedule II, the endocrinologist prescribing for him would be liable to criminal penalties. Had Dr. Blizzard or any of the early discoverers of HGH treatment been so regulated, the HGH treatment that has benefited so many hypopituitary youngsters might not have been found. What of the many non hypopit children who may benefit as well? The evidence for improvement in stature in girls with Turner Syndrome is now well-documented. I know of several IUGR (intrauterine growth retardation) babies who only grow with HGH endogenously administered through tests indicate they have their own supply, which seems to not be "bioavailable" to them. There is a large group of extremely short children, usually described as "constitutionally delayed" who are often treated with the steroid "Anavar", but who in fact might have safer and better results with HGH.

I have received up to a hundred telephone calls in a year asking me for physician referral and treatment information. Approximately 20 percent have gone on to discover their children have HGH treatable growth disorders. Considering that most callers are sophisticated enough to have found the name of our local group and the phone number, you can appreciate that most also had regular pediatric care for their children, yet the growth disorders went untreated until the parents looked further for help. The majority of parents were appropriately very cautious in initiating drug therapy and began only after considerable deliberation.

It has been estimated that for every child receiving treatment, there may be five (or even more) who remain undiagnosed. And at present etiological diagnosis is still in its infancy for growth disorders: what causes many cases of retarded growth, or growth failure, simply is not known. I have been told by physicians that a third of HGH recipients are children with hypopituitarism subsequent to brain tumors. What of the remainder? Like my son, most may be diagnosed as "growth disordered, cause unknown." They may have circulating HGH that comes and goes, but doesn't seem bioavailable. And they may have many symptoms related to their growth disorders but most of the symptoms' causes are likewise unknown. I have met many parents whose children were not treated when only biological HGH was available, because their dwarfed children's lack of endogenuous growth hormone could not be documented with the tests then in use. Most of these children grew up to be dwarfed adults with the many liabilities extreme short stature incurs. Their younger siblings benefited by newer tests and are growing thanks to HGH therapy.

If the proposed legislation is enacted, physicians will be reluctant to engage in the kind of *ad hoc* experiments on individual patients that have been so productive in the past; with drug production maximum quotas there also will be limited drug availability to perform such trials. Quotas can limit the amount of HGH available for the expected increase in the diagnosed growth disordered population as new procedures and tests are created and we learn more about how HGH interacts with other circulating blood chemicals. Quotas also eliminate the market incentive for improvement of this drug, though most parents have felt great relief that a methionine-free product, more like biological HGH, is being developed which we hope will be safer than the currently approved product.

Restriction of access to the drug harms those most in need of HGH. Many parents must travel great distances to have their children treated; were they required to make monthly treks to hospital pharmacies with repeat charges for office visits, their children's therapy might become physically and financially impossible for the parents to undertake when the costs of HGH are already so very high. Even if the direct access restrictions of Schedule II were waived for documented hypopituitary children, the majority of children with growth disorders would remain with a prohibitive obstacle in obtaining treatment. No law should so burden parents. We have been through so much already trying to find out why our children don't grow.

I believe that the committee's purpose in proposing this legislation to curb HGH abuse is praiseworthy. I appreciate that the bill's drafters have met with parent groups and listened to their concerns, and have even suggested special amendments to the operation of Schedule II restrictions that if carefully worded would hopefully eliminate the visitation and refill problems of accessibility of the drug for children with growth disorders of various types. I do not however believe that this legislation would effectively eliminate, or even retard abuse of the drug. I would like to offer for the committee's consideration a mechanism that would benefit the many children with growth disorders, and which might also restrain abuse of HGH.

The time has come for establishment of an advisory council similar to the professional diabetes council established by Congress in the 1970's under NIDDK (National Institutes of Health-Diabetes, Digestive and Kidney disorders) auspices which can direct and plan for growth disorder investigations so that controlled, cohesive studies may be undertaken. Probably such a group would best fit in the NIH Institute for Child Health and Development (NICHD) as it would plan and coordinate research across the wide range of growth disorders. I would hope it would have lay group advisors to represent the parents' concerns as well as interdisciplinary professionals because endocrine and neurological functions are vitally involved.

A Growth Disorders Advisory Council could initiate research imperatives including such questions as the role of HGH in obesity or athletic prowess (which is muscle development, strength and coordination) thus short circuiting the abusive situation and providing socially useful answers that may impact on all of us. It seems incredible that at present there are no medical studies following HGH children after they are physically grown, although a few researchers are studying psychological development. What happens to these children in maturity? Do they in fact need continued medical assistance to function normally? No one knows. As growth is the fundamental process of life, I would hope that research would also be directed at understanding why growth disorders occur. There are some forty diseases that have concomitant growth disorder and growth retardation yet no one knows why. Research that took place when HGH was administered by the NHPA was primarily physician proposed, and primarily directed toward improved treatment modalities. Most of the funds given as career starter grants likewise come from researcher proposals. There is no coordination of research, no cohesive presentation of it, no intergroup cooperation among the various specialities that may deal with the assorted symptoms. And so, we know little more today than we did 30 years ago about the real etiology of growth failure. We don't even know why endogenuous HGH may fail to produce growth yet exogenuously administered HGH often will work.

As a parent, I feel frustrated by the system. For years we begged for treatment for our child, as we were sure he needed "something". When he got treatment, and it succeeded, we were disheartened by the capriciousness of availability of the drug; he qualified to receive the minimum dosage, but a little more might have given him "catch-up growth" . . . perhaps eight inches . . . for the 5 years of no treatment. We were dismayed at the cost when finally a commercial source became available to supplement the inadequate supply. We became deeply worried at possible danger to our child when HGH was withdrawn because of the Creutzfeld-Jacob cases, and angry that NIH's Dr. Gadjusek's warnings of potential CJD contamination went unheeded for 5 years, until deaths occurred. We joined other parents to lobby for funds that might save children's lives if a thorough epidemiological survey was undertaken, and have regularly returned to Congress to add our testimony to the need to guarantee this project and maintain the necessary NIH budget that brings life and hope to so many. A growth disorder advisory council is very inexpensive. It can uncover gaps and plan for the future as no other agency can. It can provide information that would stem abuse of HGH and the related drugs I am sure will someday be available, and should it uncover valid other uses of the drug, that could only help bring down its cost and encourage further orphan syndrome investigations in the private sector.

In closing, I urge you to consider my proposal for a growth disorder advisory council under NIH auspices and table the proposed regulatory legislation for the time being. I have discussed the idea of an advisory council with a number of leading physician-researchers and they are enthusiastic about the potential of a well-chosen, interdisciplinary council to benefit their patients with growth disorders. While abuse of HGH may be immoral, the public effect of HGH regulation would be truly harmful. The proposed bill would hurt the very population for whom the drug was developed. It would result in decreased physician experimentation in valid situations and limit availability to an increased population of children recognized as being growth disordered. We parents do not need legislation to restrict access to treatment for our children. We do need laws to encourage research into what HGH can do to aid children with growth disorders and possibly to treat related conditions in which the body's natural growth regulation mechanism breaks down. I urge you to help us get the help we really need; publicly directed research is the only way to stamp out quackery and misuse of HGH.

Thank you very much for this opportunity to share my views with members of the committee.

Mr. WAXMAN. Thank you very much.

Mr. Coussan.

STATEMENT OF STEPHEN CARL COUSSAN

Mr. COUSSAN. As I said, I am Carl Coussan. I am the parent of a growth hormone deficient child, who had received both the pituitary-derived growth hormone as well as the synthetic variety.

I am also a representative of the Parent Council for Growth Normality, which is a non-profit volunteer organization of families of children who require human growth hormone for normal physical development.

Mr. Chairman, in the last 2 years, our families have been through an extraordinary situation, which has been both dangerous and extremely stressful for several reasons.

Since the early 1960's, approximately 10,000 individuals have received the pituitary hormone in treatment of growth hormone deficiency. In April of 1985, my family, along with thousands of others, was devastated by the news that three individuals had died of Creutzfeldt-Jakob disease, which was a rare and invariably fatal neurological condition. The deaths, as you know, were linked to contamination of the pituitary hormone.

This drama will be played out over the next 10 to 15 years, while we wait to see whether our children indeed were exposed or infected and whether or not they come down with this terrible and horrifying disease.

In addition to having to shoulder this incredible burden, we current parents have the strain of continuing to provide treatment for our children who are still in treatment at an incredible expense.

According to our records, our member families pay an average of about $17,000 annually for treatment with Protropin. My own son's annual expense runs slightly over $21,000. The high-end figure that we are aware of is nearly $30,000.

So in addition to wondering if indeed our children may at some point come down with C-J disease, we still are subject to all of these strains of treating a chronic illness or a chronic disability.

Left untreated, our children will definitely be inflicted with a crippling disability. We're not talking about a cosmetic situation here. We're not talk about the difference between 5′11″ and 6′2″. My own child will be 13 years old at the end of this month, and he is only slightly over 4 feet tall, this after over 3 years of treatment with growth hormone. So you can see the type of situation that we're up against.

While we appreciate the verbal assurances that have been made by you, Mr. Chairman, that the interests and the needs of our children will be provided for, you must excuse our skepticism.

In the last 2 years, we have been treating out children with a product that we were originally assured was entirely safe, without side effects, a natural body substance. Because of that treatment, we now live under the shadow of a fatal, incurable disease.

We were originally told that the synthetic hormone would be advantageous to us, because it had the possibility of being much cheaper. I have media articles which refer to the annual cost as being $5,000 to $6,000. With the bills that I see on a quarterly basis, that statement is laughable at this point.

We were told that the research to determine what the risk factor of C-J to our children might be would be immediately underway, instead we find ourselves each year fighting for those appropriations before the appropriate subcommittees.

We depend on no one but ourselves at this point. We know that if we want to obtain the treatment that is necessary for our children, if we want to make sure that it is safe and efficacious, if we want to make sure that we had adequate affordability, adequate accessibility, that we have to take the issue into our own hands and do what can be done.

So you will excuse our natural skepticism, I hope, in terms of what public policy might be.

We are concerned that our children become the main and primary focus of public policy on the growth hormone issue. It frankly galls us that the motivation for this legislation and many other forms of public policy regarding growth hormone has as its primary focus other groups than our children, who are, after all, the main reason for the existence of this drug, the only legitimate reason for the existence of this drug at this point in time. And at this point, we can only hope that you will continue to consider our children as the primary focus.

It is not longer enough mainly for public policy to be benign in relation to what our children's needs are. We have to be assured that our children will be the primary focus in ongoing treatment.

Thank you.

[The prepared statement of Mr. Coussan follows:]

TESTIMONY OF STEPHEN CARL COUSSAN, PARENT COUNCIL FOR GROWTH NORMALITY

Mr. Chairman, I am Stephen Carl Coussan, parent of a growth hormone deficient child, and representative of the Parent Council for Growth Normality (PCGN), a non-profit, volunteer group organization of parents whose children require human growth hormone (HGH) for normal physical development. It is my intention to present to the subcommittee the concerns of our families regarding the proposed changes in the regulation of synthetic (recombinant) HGH, and to provide some insight into the plight of those who, for good or ill, will be most affected by its decisions. A common threat in the history of HGH treatment has been the creation of policy for research, modes and delivery of treatment, and administration and oversight in an environment which isolated the patient-consumer and discouraged participation in decisions that intimately affected health and quality of life. We are grateful to the subcommittee for the opportunity to express our concerns as a part of the process, rather than merely its subject, and urge you to remain mindful that your deliberations may affect our children for the rest of their lives.

Growth Hormone Deficiency—Left untreated, the HGH deficient child will fall far short of five feet in adulthood. Studies have documented the stresses on these children and their families emotionally, socially, academically, and environmentally. In addition, growth hormone is necessary to proper functioning of the body's metabolism, a life-threatening concern to the percentage of HGH children who are hypoglycemic. Fortunately, our children's disability is correctable, with injections of replacement hormone enabling them to approach normal adult height. Our sense of urgency in providing uninterrupted treatment will be clear, however, when it is realized that HGH is only effective until the long bones close during puberty, at which time no further height gain is possible.

Treatment Background—Since the 1960's approximately 10,000 Americans were treated with HGH refined from human pituitaries harvested during autopsy. On April 19, 1985, our families were devastated by the news that three former hormone recipients had died of Creutzfeldt-Jakob disease (CJD), a rare, degenerative, invariably fatal neurologic disorder for which there is neither treatment nor cure. The deaths were linked to contamination of hormone produced and distributed by an agency of the National Institute of Diabetes, Digestive, and Kidney Diseases (NIDDKD) by the viral agent thought to cause CJD. In response to the crisis, the FDA halted distribution of the NIDDKD hormone, as well as the two extant commercial products. Children then in treatment were left facing the spectre of exposure to an incurable disease, and with no safe source of the product they desperately needed. The hiatus in treatment, critical time that may never be recouped by our children, continued until October, 1985, when a synthetic HGH product, *Protropin* from Genentech, gained FDA market approval. *Protropin* remained the sole source of treatment until March, 1987, when a second recombinant product from Eli Lilly was approved.

Parental Concerns—In a situation replete with inconsistencies and shifting focal points, our concerns on behalf of our children remain constant and unswerving: they require a safe, efficacious source of growth hormone, readily available to all growth hormone deficient children, which our families can reasonably afford to provide. We must, therefore, consider every action, including the proposed regulation changes before this subcommittee, in light of these concerns. While potential misuse or abuse of any drug is of interest to responsible citizens, we strongly feel that the primary focus of any legislation regarding HGH should have as its first priority the protection of the legitimate medical needs of the patient population. In this instance, our children are the only current legitimate recipients of recombinant HGH, and, indeed, are the reason for its existence on the market. While we, as parents, realize that this proposed legislation was not aimed at harming our children, neither was it aimed at helping them; in fact, our children's medical needs did not enter into consideration of these proposed regulatory changes. Therefore, Mr. Chairman and members of the subcommittee, we urge you to carefully consider all the possible implications of this bill as it may affect our children's treatment and, ultimately, the rest of their lives.

Safety and Efficacy—We are deeply concerned about the possible chilling effect of Schedule II status on ongoing research into growth hormone therapy. Although recombinant HGH does not carry the risk of biologic contamination inherent in the pituitary-derived products, long-term issues of safety and efficacy have yet to be resolved. It is sobering to consider that, despite 20 years study with 10,000 individuals, the pituitary HGH experience ended in disaster, to be replaced by a product tested for 7 years on fewer than 100 patients. Already living with one medical tragedy, we cannot help but fear that any regulation which would tend to depress widely-based, ongoing research may work to the detriment of our children.

Research and Siagnostics—In classing recombinant HGH with drugs such as morphine and *Dilaudid*, Schedule II status may well serve to make researchers, physicians and parents reluctant to pursue HGH study and treatment with HGH deficient children. Current diagnostic methods for determining HGH deficiency are often imprecise and inconclusive. In many cases, including our own, diagnosis becomes a combination of observations of retarded bone age, abnormally small stature, certain physical characteristics, and very borderline, inconclusive lab test results. Growth then becomes the ultimate diagnosis: the child is usually put on HGH therapy for a quarter (3 months), and growth is closely monitored. Response to HGH injections is then considered the final diagnosis of HGH deficiency. In associating HGH in the minds of parents and physicians with "frightening" drugs, how many children will fail to receive treatment, turning a correctable problem into a life-long disability? The Catch-22 for our children is that, without continuing research and study, diagnostic methods will not improve for lack of data.

Availability—The demographics of growth hormone therapy are almost entirely restricted to regional centers, to which HGH deficient children and their families travel on a quarterly basis (four times annually). Genentech has been very sensitive to the suggestion of potential misuse of their recombinant product, and has limited distribution to hospital pharmacies connected to these centers, and to a health care delivery system where no hospital pharmacy access is available. Eli Lilly has indicated that they plan to follow much the same plan of restricting distribution. Both companies have taken what we feel is a very responsible and circumspect position in restricting availability only to those who should legitimately receive their products. Under the proposed Schedule II designation, parents and children would have to travel to regional treatment centers not four but *twelve* times a year to receive their HGH prescriptions, with a resultant three-fold loss of school and work time, and home health care delivery would become more difficult and restricted for all of us who must depend on this method of access. It is difficult for us, as concerned parents who will reap the additional hardships of this legislation, to envision that the potential benefits of this proposed bill are so superior to the restrictions voluntarily adopted by the pharmaceutical companies as to outweigh adverse impact on our families.

Affordability—Although early indications were that recombinant HGH would be considerably less expensive than the commercial pituitary HGH, higher recommended dosage levels and changes in the system of delivery have produced to-the-patient costs that average $17,000 annually among our membership—costs which escalate dramatically as dosages increase with the onset of puberty, and the inevitable end of effective treatment approaches. There are several vital points which must be considered in assessing the issue of affordability and in understanding our viewpoint as parents of the patient population. The first is that the vast majority of those being treated with pituitary HGH received it free-of-charge through an agency of NIDDKD—thousands of us must now find the means to cover an additional medical expenditure averaging $17,000 each year. The second is coverage. Although all but one State now offers Medicaid coverage and/or Crippled Children's coverage, and although most insurance carriers offer at least some reimbursement, these statements do not present an accurate picture of the facts. They do not reflect the calls and letters to achieve that Medicaid coverage. They do not reflect the fights with reluctant carriers and the families who had to change carriers or afford additional coverage to receive a level of reimbursement with which their families could function. Not only the pharmaceutical companies involved in this issue, but also a sampling of physicians and pharmacists around the country have indicated that the increased handling and paperwork inherent in Schedule II classification would be likely to cause a price increase in recombinant HGH. Aside from the additional, for many unbearable, financial burden this would impose on our families (at present, a fairly standard 80 percent coverage results in $3,400 out-of-pocket each year), any substantial increase as a result of this bill would likely cause the battle with Medicaid and private carriers to begin all over again.

In Summarization—Our experience with HGH therapy has, unfortunately, taught us to take nothing for granted where our children's welfare is concerned. We had a product we were assured was a safe, natural body substance, and instead found our children living under the shadow of a horrifying, incurable disease. We were assured the matter was duly under study, and found ourselves fighting for study funding before the Appropriations Subcommittees. We were told throughout the media that our new, safe alternative to give our children a normal life would be less expensive, yet find ourselves struggling with an increasing financial burden. You will, I hope, forgive our skepticism in accepting assurances that this proposed bill would have little effect on us and on our children, the only current legitimate market for recombinant growth hormone. We fail to see that any benefits to be derived from stemming a theoretical, undocumented flood of abuse can outweigh the hardships we envision as resulting from this legislation.

As responsible, intelligent people we are, of course, concerned with the question of possible misuse or abuse of the exiting new technology these recombinant products represent. However, as intelligent, responsible parents, we fail to see that this proposed regulatory change in any way benefits or protects our children, whom these products were created to help. Mr. Chairman, members of the Subcommittee, you may view our concerns as speculation on the possible effects of this bill. I must point out to you that the issue of misuse/abuse is equally speculative. The difference is that, should you pass this legislation and the issue of abuse never arises, no one is the lower. Should you pass it and *our* fears are realized, thousands of our children are the losers.

Considering what we've been through in the last 2 years, it is indeed ironic that it has been suggested, in some quarters, that our fears are a product of manipulation by the pharmaceutical industry. Mr. Chairman, we remember our innocence, but that memory is ever-fleeting.

While we are sensitive to the broader issues implicit in this proposed legislation, the welfare of our children must remain our primary focus, and that of this Subcommittee. We respectfully request that you consider our children as the most important component in any proposal regarding growth hormone, and that you carefully consider the implications and ramifications of any such legislation, on behalf of all our children.

Mr. WAXMAN. Thank you. I want to thank you both. You've been excellent witnesses in telling us the perspective that we cannot forget as we deal with this whole question. After all, we're talking about a drug that we hope is going to be a successful replacement for its predecessor that turned out to be so frightening in its consequences, and for which you were faced with not only the threat of another disease, but a threat of shortages when that drug was pulled off the market.

So I fully understand what you're saying. And furthermore, what we're dealing with are people who are going to take this drug and use it in ways for which it was never intended. They're doing it theoretically under their own volition, with their own knowledge and free will, but in fact with very little information for them to determine whether it is going to be beneficial to them and whether there are possible side effects. We don't now yet whether it's beneficial to them in terms of what they hope to achieve. But any reasonable person would have to come to the conclusion that it's not worth taking a drug for athletic purposes, where it is perfectly reasonable for the purposes you're concerned about.

So I would not be, in any way, for legislation that would hinder your ability to get this drug for the purposes that your children need it for. And as we think through any kind of a balance, that clearly has to be our overriding concern. I fully agree with you.

Mr. COUSSAN. Mr. Chairman, I think our main consideration in terms of whatever amendments are written into the bill in terms of access for growth hormone deficient children is as to how growth hormone deficiency would be defined, what the parameters might be, and who would—whose responsibility would it be to set those parameters.

I think that, as Mrs. Chadwick said, a certain amount of leeway needs to be considered. A substantial number of our children cannot be specifically diagnosed as being growth hormone deficient.

And yet for them, treatment is the ultimate diagnosis. We know that they're disabled when they're small. Without growth hormone, they do not grow. With growth hormone, they grow.

And yet if you're looking for something that can be quantified on paper in this instance, you probably don't have it. My own son falls into that category.

And as I said, treatment is the ultimate diagnosis, and it's a very sensitive issue that we would ask you certainly to be very aware of in terms of setting the parameters there.

Mr. **Waxman**. That's a good point. Wherever we draw the line, we want to make it clear that for legitimate therapeutic purposes, for legitimate medical purposes, that this drug would be available.

Mr. **Coussan**. I'd like to interject one other thing, if I may, Mr. Chairman.

Remarks have been made in various circles as to what specifically my relationship may or may not be with the pharmaceutical companies and the pharmaceutical industry in general.

I have to take very strong issue with those remarks. Our organization is all volunteer. We have no professional staff. We have no funding whatsoever from any of the drug companies or outside sources, other than the generosity and motivations of our own families. It's run from a kitchen table, on a personal telephone. When I come to Washington from Louisiana, I am here at my own expense, for my own child and for the other children like him.

At various times, it has been suggested that parents are incapable of rendering objective judgment and objective testimony on this issue because of our emotional involvement and because we are too susceptible to the scare tactics that might be used by the drug companies.

With what we've been through in the last 2 years, Mr. Chairman, I remember innocence, but it's a fleeting memory at this point. We remain skeptical of all of the parties involved in this particular issue, whether they be public or private or medical or scientific. And I think at this point that was something that needed to be said, and I appreciate your indulgence there.

Mr. **Waxman**. Well, I understand what you're saying. And let me tell you, from my own experience as Chairman of this subcommittee, over and over and over again, we've had hearings on various illnesses and diseases, and the thing that comes most to my mind is when we dealt with the orphan drug issue.

But the experience that is clear to me is that the people who end up knowing more than all the so-called experts are the family members, and so often when they find someone in their family afflicted by some kind of illness or disease, and they look around for help, all the people you'd expect would know just don't know. And the support groups aren't often there. And when the support groups are there, they're set up by the family members for others who are going through the same experience.

So I have a very clear understanding of what you're saying and a healthy regard, admiration, and respect for the people who are living with these various issues on day-to-day basis. I wanted your input, and I appreciate your testimony. If we're going to do any legislation, I want you to review it and talk to me further about it, because I in no way want to do anything that is going to be to your children's disadvantage.

So I thank you very much.

Yes, Ms. Chadwick, do you want to add one thing? I know you've been here all day, however. There's another meeting I'm supposed to attend.

Mrs. CHADWICK. I just have a genuine concern about the quota aspect that I think, in writing whatever your committee will ultimately write, that should be concerned. There is a whole realm of children who might be 5 feet tall for whom this drug might be a specific cure for what is actually an extreme short stature disorder, and these would not be the same cosmetic individuals that we're talking about making into basketball players, but these would be children with constitutional delay syndrome or nothing specific, but they are just a little behind in bone age.

They need to have some help, and this would help them. It would help them psychologically by helping them physically at a younger age.

There has been a steroid drug called Anavar used for decades for this group of children. The purpose of that drug was to speed up their growth, but it had negative side effects. Human growth hormone looks as though it would work for those children, but there is no historical example of that use, so that if you built a quota based on prior usage, you would be building an inadequate quota to this potential and a few other potential populations.

The reason that there was no prior use was because biological hormone was not available.

Mr. WAXMAN. Sure.

Mrs. CHADWICK. This drug, the biosynthetic drug, is available, and that's what makes it so exciting and important to parents, that it's now there for the first time for them. That's been the case with my son, with Carl's son, and with many, many children that we know who simply did not grow before.

Thank you.

Mr. WAXMAN. That's a very good point, and thank you for it.

We're going to leave the record open for this hearing for 2 additional weeks to receive any further thoughts that any of you have, any testimony that others want inserted in the record, and any statement from members of the subcommittee.

Mrs. CHADWICK. Is it possible to invite a pediatric endocrinological group, whom we have not heard from at all, rather than just the sports medicine physicians, since that's the group that does all of the prescribing for this drug?

Mr. WAXMAN. That's one of the reasons we're going to keep the record open, so that we can get that additional information.

Thank you. That concludes our hearing for today. I thank everybody for your participation in it, and we will look forward to talking further and working with you.

[Whereupon, at 2:45 p.m., the hearing was adjourned, subject to the call of the Chair.]

[The following statements were received for the record:]

STATEMENT

of the

AMERICAN MEDICAL ASSOCIATION

to the

Subcommittee on Health and the Environment
Committee on Energy and Commerce
United States House of Representatives

RE: Scheduling of Human Growth Hormone
Under Schedule II of the Controlled Substances Act

April 22, 1987

The American Medical Association takes this opportunity to comment on the issue of whether human growth hormone (HGH) should be scheduled under schedule II of the Controlled Substances Act.

Comments

Recent advances in biomedical research now permit the synthesis of human growth hormone by recombinant DNA technology. This advance has permitted the production of a growth hormone that is free from viral contamination and, at the same time, is identical in its physiological activity to the naturally occurring hormone. The enhanced capacity to "manufacture" human growth hormone assures access to the definitive treatment for growth hormone deficiency for all children who need this important drug. However, in addition to this proven therapeutic benefit, it has been stated that HGH may be misused or abused by athletes and others in order to attempt to increase their size and strength.

The AMA opposes legislation that would schedule HGH under the Controlled Substances Act. The proper route for scheduling a drug is through the well-developed regulatory process -- not by legislation. We also believe that scheduling HGH administratively under schedule II would be inappropriate. HGH does not meet the criteria for scheduling under schedule II of the Controlled Substances Act in that it does not "lead to severe psychological or physical dependence" (emphasis added), as required by Section 202(b)(1)(C) of the Act (21 U.S.C. 812(b)(1)(C)). In addition, the Controlled Substances Act, heretofore, has included only those drugs whose abuse potential proceeds directly from their psychoactive or psychotropic effects. The inclusion of an "atypical" compound such as HGH is a major change in policy that demands in-depth study. Finally, we are concerned that inclusion of HGH in schedule II could serve to restrict the availability of the drug for those children who truly need it and could impede important research.

Regulatory Mechanism for Drug Scheduling

The appropriate avenue for scheduling a drug is through the well-established administrative process. The Controlled Substances Act authorizes the Attorney General, through the Drug Enforcement Administration (DEA), to initiate proceedings to schedule or reschedule a drug or to remove controls on a drug. Before action can be taken, the Attorney General must request a "scientific and medical evaluation" of the drug from the Secretary of Health and Human Services through the Food and Drug Administration (FDA). The FDA also makes a recommendation as to whether the drug should be controlled (and if so under what schedule) or removed from the schedules. If the DEA concludes that the information provided by the FDA constitutes substantial evidence that a drug has potential for abuse, it must initiate proceedings to schedule it. If, however, the FDA recommends that a drug not be controlled, the DEA is not allowed to control it. Finally, if the data provided by FDA constitutes substantial evidence that a drug should be removed entirely from the schedules, proceedings for removal of the drug must be initiated by DEA.

This regulatory mechanism, which relies heavily on the expertise of the FDA and DEA, has proven to be highly satisfactory in reviewing and evaluating drugs. No convincing reasons exist to forego this process set up by Congress in favor of direct legislative rescheduling. The legislative process would inappropriately preempt a well-developed program designed to deal specifically with the scientific, medical and regulatory issues.

Scheduling of HGH is Inappropriate

The factors that the FDA must consider in making its recommendation concerning whether a substance should be controlled include:

1) the drug's actual or relative potential for abuse;
2) its history and current pattern of abuse;
3) the scope, duration and significance of abuse; and
4) the risk, if any, to the public health.

We do not believe that these criteria have been met.

While the AMA recognizes that HGH has a limited potential for abuse, little or no data exist that substantiate or define a history, pattern, scope, duration or significance of abuse. Nor is there reliable evidence to indicate that HGH poses any significant risk to the public health. Finally, data to substantiate a relative abuse potential similar to other schedule II drugs - such as cocaine - is lacking. Thus, we believe that if the FDA were to conduct a rigorous "scientific and medical evaluation" of HGH, it would conclude that the drug should not be controlled under schedule II at this time.

We question whether it is appropriate to regulate, under the Controlled Substances Act, substances for which the basis for abuse potential is not psychoactivity. At present, all compounds included under the Controlled Substances Act derive their reinforcing properties, abuse potential, and capacity for producing psychological and/or physical dependence directly from their effects on the central nervous system. Human growth hormone, however, is released from the anterior pituitary, outside the central nervous system, and its most direct effects are on physiological systems other than the central nervous system. Indeed, the claimed potential for abuse is unrelated to any psychoactive or psychotropic effect.

Human growth hormone represents the second major medical product produced by recombinant DNA technology. This technology proffers many great advances for medicine. Many of its products will be endogenous hormones that serve to replace or correct deficiencies extant in specific patient populations. This capacity to produce biological products identical to modulators of all types of human functions is raising important scientific, clinical, ethical and legal issues. It is important for appropriate resolution of such issues that credible scientific and clinical evidence constitute the basis for the decisions that address such issues -- not anecdotal reports and vague concerns.

We are also concerned that the rigid production and distribution controls for schedule II drugs could serve to impede the availability of HGH for those children who truly need the drug. We believe strongly that the benefit of enhanced availability of HGH to those with serious medical problems far outweighs any risk posed to the public health by anecdotal reports of "abuse" of the drug.

Finally, wider therapeutic applications of HGH are now being studied. Inclusion of HGH under the controls of the Controlled Substances Act, particularly under schedule II, could restrict valuable research.

Conclusion

The AMA opposes legislation that would schedule HGH under the Controlled Substances Act. The proper avenue for scheduling a drug is through the well-established regulatory process, not by legislation. In addition, scheduling HGH under schedule II would, at this time, be inappropriate. HGH does not meet the criteria for scheduling under schedule II of the Controlled Substances Act. Moreover, the Controlled Substances Act, heretofore, has included only those drugs considered psychoactive or psychotropic. The inclusion of an "atypical" compound such as HGH is a major change in policy that demands in-depth study. We are also concerned that rigid quotas for schedule II drugs could impede the availability of HGH for those children who truly need the drug. Finally, we are concerned that inclusion of HGH under the Controlled Substances Act, particularly under schedule II, could serve to curtail important research on the drug.

REPORT OF THE COUNCIL ON SCIENTIFIC AFFAIRS

Report: B
(I-86)

Subject: Drug Abuse in Athletes: Anabolic Steroids and Human Growth Hormone (Resolution 57, A-86)

Presented by: John H. Moxley, III, M.D., Chairman

Referred to: Reference Committee E
(E. Robert Tyson, M.D., Chairman)

This report, the first in a three-part series on drug abuse by athletes, responds to adopted Resolution 4 (A-84) and to Resolution 57 (A-86), "Human Growth Hormone," which was referred to the Board of Trustees for action. Subsequent reports will cover other classes of abused drugs.

Introduction

The problem of misuse of anabolic hormones (both steroids and growth hormone) is complex and can be considered from different perspectives:

(1) Psychological:

- (a) The importance of winning;
- (b) Placebo effect of drugs.

(2) Pharmacologic:

- (a) The possibility that these hormones may provide a real physiologic advantage for the athlete;
- (b) The adverse effects of such misuse.

(3) Ethical:

- (a) The concept of violation of fair play;
- (b) Implicit coercion to use drugs in order to be competitive;
- (c) The concept of hormonal manipulation, particularly in children, to alter body size and build in a manner perceived to be beneficial for athletics or other life endeavors.[1]

Past House Action: A-86:371; A-85:282; A-84:334; A-79:277; I-79:45-47; A-79:277; A-72:261,384

General solutions to the problem range from prevention (eg, regulatory action limiting production and/or distribution of drugs) through symptomatic treatment (eg, drug testing of competitors) to cure (eg, motivation of the individual to reject drugs). The personal decision to reject or discontinue drug use is based on the individual's values and reasons for considering drug use. Hence, an ethical argument based on the concept of fair play may be ineffective in an individual who is motivated to win at any physical cost.

Anabolic steroids and growth hormone will be discussed separately. The following questions will be considered for each:

(1) Does the drug provide real or perceived benefit for the athlete?

(2) What are the adverse effects of the drug in this setting?

(3) Who promotes, distributes, and uses the drug?

(4) Is abuse of the drug a significant problem?

Anabolic Steroids

Anabolic steroids are synthetic androgens that have greater anabolic relative to androgenic activity than testosterone, but in large quantities, these drugs have strong androgenic effects. In general, they are not as useful and effective as earlier thought, but do have legitimate uses in several conditions (eg, certain anemias, hereditary angioedema, breast cancer, and possibly osteoporosis).

Anabolic steroids have been used by athletes for more than two decades in the belief that they increase body mass, muscle tissue, and strength. More recently, testosterone has been used because it is more difficult to detect in drug screening programs than anabolic steroids. Although studies of these agents have not shown uniformly increased muscular strength, certain benefits to athletic performance seem probable: increased body weight, partly due to fluid retention, may include increase in lean muscle mass. In a continuing program of intensive exercise coupled with a high protein diet, increased muscular strength may be realized in some individuals. In contrast, aerobic capacity is probably not increased beyond that due to aerobic training.[2,3] Increased aggressiveness is also reported among anabolic steroid users, but the degree to which this influences the intensity of training is unknown.[4] It should be noted that small, difficult-to-measure increments in muscular performance or psychological benefit may constitute the difference between winning and losing, particularly at a professional or world-class level. Therefore, these changes may be perceived to be critical to an athlete.

There are clear adverse effects associated with use of androgenic steroids. The doses and patterns of administration utilized by athletes often differ markedly from those used therapeutically. Athletes have been reported to take steroids cyclically for one to several months followed by a drug-free period up to a year. Doses may be far greater than those considered to be therapeutic, and drugs are sometimes "stacked" (several agents taken simultaneously).[5] Exogenous androgens affect the reproductive system of healthy males: gonadotropin and testosterone secretion are suppressed and oligospermia and temporary infertility may occur. Gynecomastia is common.[6] Agents that are 17 - alkylated compounds (eg, oxandrolone, methandrostenolone) are associated with liver pathology, including abnormal liver function tests, cholestasis, peliosis hepatis, hepatic adenomas, and hepatocellular carcinoma.[7] Although hepatic effects have been described and documented most often in patients treated for disease, one case of hepatocellular carcinoma has been reported in an athlete who had taken several anabolic steroids to increase skeletal muscle mass.[8] Anabolic steroid ingestion by athletes is also associated with an atherogenic blood lipid profile (eg, elevated low-density lipoprotein cholesterol and decreased high-density lipoprotein cholesterol).[9] Increased irritability and aggressiveness may occur.

In women, androgenic hormones produce masculinizing effects (eg, hirsutism, deepened voice, oily skin, acne, male pattern balding, menstrual irregularities, increased libido). In children, these drugs may accelerate pubertal changes and limit eventual adult height by causing premature skeletal maturation and closure of the epiphyses.

Steroids apparently are used at all levels of athletic activity. Although the prevalence is difficult to assess accurately, such use is believed to be widespread.[10] Steroid abuse is particularly common among athletes in strength sports (eg, weight lifters, body builders, shot putters, and discus and javelin throwers). Use among weight-trained women athletes has been reported. Anabolic steroids have a more significant effect on female muscular development than on males. In one study, the women reported typical masculinizing side effects, which they considered an acceptable price for the anabolic benefits.[11] A particular concern is that the wide availability of these agents is likely to make them accessible to adolescents and children, as well as adults.[12]

Anabolic steroids are easily obtained on the black market through gymnasiums or mail order sources. In a survey of 250 weight lifters, almost half admitted using steroids at some time. Although most steroids were obtained illegally, some athletes claimed that they had been given a prescription for the drugs.[13]

In 1985, the Food and Drug Administration (FDA), Federal Bureau of Investigation (FBI), and Department of Justice (DOJ) began a nationwide criminal investigation of black market distribution of anabolic steroids and other drugs purported to enhance athletic performance. Manufacturers and distributors were advised of their responsibility to ensure distribution only to authorized customers and were requested to monitor and report unusual order activity (eg, large or frequent orders, orders by pharmacies for veterinary products). Indictments have been obtained as a result of this effort.

Growth Hormone

Human growth hormone (hGH) or somatotropin is a polypeptide hormone secreted by the anterior pituitary gland. GH has widespread metabolic effects, including stimulation of cellular amino acid uptake and protein synthesis, stimulation of lipolysis, and inhibition of glucose utilization in tissue, which tends to increase blood glucose levels. Growth hormone is necessary to achieve normal genetic growth potential. Severe deficiency in childhood results in dwarfism. Human GH is necessary to treat this condition, because GH from other species is ineffective.

Human pituitary-extracted GH was available from the National Hormone and Pituitary Program and commercial sources until 1985. After the appearance of several cases of Creutzfeldt-Jakob disease believed to have been caused by contaminated pituitary extracts, distribution of the product was halted voluntarily for an indefinite period. Following withdrawal of the pituitary products, a recombinant DNA-derived GH product was approved for marketing in the United States. It is identical to endogenous hGH except for the addition of methionine on the N-terminus of the molecule. This preparation is available commercially.

The results of hypersecretion of hGH are of particular interest in the context of this report. Uncontrolled hypersecretion in childhood results in gigantism, and in adulthood, acromegaly. The latter condition is associated with glucose intolerance, heart disease, impotence, and bony overgrowth (eg, protruding forehead and jaw, enlarged hands and feet).

Adverse effects of hGH use by athletes have not been documented but can be predicted on the basis of known effects of endogenous hypersecretion (vide supra). Whether limited exogenous administration may produce beneficial or deleterious effects in healthy athletes is unknown. The effect of hGH administration to normal children is unknown, but might be expected to produce a permanent increase in build and stature. Beyond the physiologic considerations, use in normal children is an ethical problem of far-reaching proportions.[1]

In contrast to the problem of anabolic steroid abuse, hGH abuse, to the extent that it exists, is a relatively new phenomenon. Reports of its use in athletes are anecdotal;[15] they suggest that hGH is currently favored because of anticipated body growth and increased strength potential and also because it is undetectable in current drug testing procedures. Use is probably limited by the great expense of the product.

The source of illicit supply is questionable. One physician reportedly obtained supplies of pituitary-extracted hGH simply by mailing prescriptions to companies supplying the product.[16] This account is inconsistent with the companies' stated distribution policies, which required screening of requests and documentation of need. Bogus hGH preparations, animal GH preparations, and foreign products should also be considered as potential illicit sources. To knowledge, there have been no reports verifying that the GH products bought by athletes are in fact hGH.

Since withdrawal of pituitary-extracted hGH from the US market in 1985, the only U.S. source of hGH is the recombinant DNA product. Although the technology to mass-produce hGH is available, the manufacturer states that it limits production and follows rigorous screening and post marketing surveillance procedures to verify legitimate use in GH-deficient patients.

In summary, the status of growth hormone abuse is undetermined, but the agent has wide abuse potential, particularly if pharmacologic benefits are shown to result from use in normal athletes. Human GH also may have additional legitimate therapeutic applications for other growth disorders, fractures, burns, and other conditions. Research in these areas has been hampered by the limited supplies of hormone available, but is expected to be undertaken in the future now that it is possible to produce unlimited quantities of the hormone. Increased availability of hGH for other legitimate uses presumably would increase accessibility for illicit use.

Conclusions

Abuse of anabolic products by athletes differs in the two types of drugs discussed. Anabolic steroids have therapeutic benefits for certain conditions and proven abuse potential among athletes. The abuse of hGH is a recent phenomenon of undetermined extent. Human GH has a clear therapeutic application in growth hormone deficiency and other legitimate investigational uses, and also has great potential for misuse.

This report responds directly to concerns regarding the abuse of anabolic steroids; future reports will deal with other classes of abused drugs. The report also addresses the issue of the abuse of human growth hormone, which was raised in referred Resolution 57

(A-86). Recommendations for AMA action will be developed after completion of all reports on drug abuse in athletes. The following possibilities will be considered in developing the recommendations:

1. Regulatory action (for anabolic steroids and growth hormone):

   The AMA should continue to endorse current activities of the FDA, FBI, and DOJ directed toward curbing illegal distribution of these drugs. If these efforts are ineffective, the AMA should undertake a study of alternate methods of monitoring and limiting distribution.

2. Educational action (for drugs with abuse potential):

   The AMA should endorse educational activities at various levels including sports group administrators, coaches, parents, and athletes. Activities suggested for consideration are:

   a) Preparation and distribution of educational pamphlets on drug abuse in athletes emphasizing the adverse effects and limited benefits of such use.

   b) Development of a nationwide network of physicians who would be available to give presentations on this topic to interested community groups.

   c) Preparation of a videotape(s) on drug abuse in athletes for distribution and use by schools, sports programs, parent groups, and community organizations.

   d) Judicious use of the news media and editorials and articles in AMA publications to publicize the AMA's interest and availability to work on this problem.

The Council on Scientific Affairs recommends the adoption of this report in lieu of Resolution 57 (A-86).

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STATEMENT OF
ARES-SERONO REGARDING

I am Thomas Wiggans, President of Serono Laboratories of Randolph, Massachusetts. Serono Laboratories is the United States subsidiary of Ares-Serono, an international developer, manufacturer, and distributor of pharmaceutical products. On behalf of Ares-Serono and Serono Laboratories (collectively referred to as Serono), I thank the Subcommittee for keeping the record open to allow Serono to submit its comments concerning the scheduling of human growth hormone (hGH).

Serono has had a long-standing interest in human growth hormone. In the early 1960s, the company engaged in some of the pioneering research that resulted in identification of hGH in the human pituitary gland. In 1973, the government of Switzerland approved the commercial sale of Serono's hGH product. Subsequently, Serono received approval for its hGH drug product in sixteen other countries. Serono began to sell pituitary-derived hGH in the United States in 1980. Called Asellacrin®, this product remained on the market until 1985, when Serono voluntarily stopped selling its product due to reports that pituitary-derived hGH supplied by the National Hormone and Pituitary Program may have caused a rare disease in patients. (No cases associated with Serono's hGH product have been reported anywhere in the world.)

Beginning in 1980, Serono began to study the use of biotechnology to produce hGH. Clinical trials with the biotechnology-derived hGH for use in treating growth hormone deficiency started in 1986. Data from these clinical trials are being analyzed, and Serono intends to submit in the near future an application to obtain FDA approval to market its recombinant hGH.

Thus, Serono has had substantial experience with human growth hormone. Based on this extensive familiarity with hGH, Serono believes that the product should not be subjected to the restrictions of the Controlled Substances Act.

First, in our view, scheduling hGH simply is not appropriate under the Controlled Substances Act. This statute was enacted to control the non-medical uses of products that are either physically or psychologically addicting. Human growth hormone is not addictive in any sense. The Controlled Substances Act was not designed to regulate products because of the possibility they might be used for unlabeled medical indications. Forcing hGH into the same regulatory category as psychoactive agents would disrupt the structure of the Controlled Substances Act and place an unwarranted stigma upon a non-addictive drug.

In addition, placing hGH in Schedule II would impair access to the product for children suffering from growth hormone deficiency. Many pharmacists refuse to stock Schedule II drugs because their presence makes the pharmacy a target for burglars. Indeed, having a scheduled drug on hand is believed by many pharmacists to place them in personal danger. Similarly, some ethical physicians prefer not to prescribe Schedule II drugs because of the stigma attached to such products.

Moreover, there are significant costs associated with scheduling any drug. The manufacturer must keep many more records, store the product separately, and face frequent audits by the government. If hGH were placed in Schedule II, Serono anticipates that additional personnel would need to be hired to ensure compliance with all the paperwork requirements of the Controlled Substances Act. Similarly, the prescribing physician and the pharmacist also need to prepare and keep additional records. Prescriptions must be completed, in triplicate, every thirty days. Some of these labor and paper processing costs inevitably will be passed on to the patient.

Scheduling hGH may also essentially preclude some patients from receiving hGH. Under the Controlled Substances Act, prescriptions may only be written for a thirty-day supply of the product. In the entire United States, there are only 300 pediatric endocrinologists. Virtually all prescriptions are issued by these doctors. Because of the paucity of pediatric endocrinologists, many growth hormone deficient patients and their parents must travel great distances to be examined by their physician. For example, in Serono's recent clinical trial with recombinant hGH, 14 of the 60 patients were required to make round trips of 80 miles or more to see their physician. Nine of the 60 patients made round trip journeys of at least 200 miles to visit their pediatric endocrinologist, and for 6 of the patients the round trip mileage was over 400 miles.

Requiring that this trek be made every thirty days could interpose almost insurmountable barriers to receiving treatment for many children. In addition to the inconvenience and lost time, there would also be the enormous additional costs of repeated examinations by doctors and nonreimbursable travel expenses.

Modifying the Controlled Substances Act to reduce the frequency of physician visitation for hGH patients would provide only minor relief. Even four to six visits a year would be prohibitively expensive for many families. Imposing these costs and hardships on the families of children who need hGH to attain normal height would be unfair and unjust. One can also question the desirability of having the United States' pediatric endocrinologists spend their time and skills on medically unnecessary examinations.

Moreover, it is far from clear that scheduling hGH would have the intended consequences. Putting a drug in Schedule II does not prevent unethical doctors from prescribing the product, or unethical pharmacists from dispensing the drug. Although the scheduling of addictive products has reduced their availability for illegal or unethical use, experience has unfortuantely shown that scheduled products are still often readily available. Indeed, the placement of a drug in Schedule II sometimes increases its allure to criminals.

Based on its lengthy experience with hGH products, Serono strongly questions the basic assumption that would underlie any legislation: that there is widespread misuse of hGH. During the five years in which Serono distributed Asellacrin®, the company became aware of only one case in which the product was available for use by individuals other than growth hormone deficient children. Serono cooperated fully with the Federal Bureau of Investigation in its investigation of the case. The individuals involved were detected, and successfully prosecuted by the United States Attorney for the Central District of California.

Serono also learned of several reports in Texas of the sale of counterfeit Asellacrin®. The company aided the FDA in investigating this situation, and the FDA has initiated litigation against the individuals involved. Scheduling hGH would not affect the ability of individuals to attempt to pass off a counterfeit product as the genuine article.

Thus, of the tens of thousands of vials of Asellacrin® that Serono distributed, only extremely small amounts of the actual product are known to have been in the possession of individuals other than those who were receiving the product for its indicated medical purpose. And, even without scheduling, the one known incident of product misuse culminated in successful prosecution.

One reason why Asellacrin® was obtained only by children in need of hGH was Serono's Patient Dosing Program (PDP). Under this program, Serono's marketing personnel would obtain substantial information from the treating physician about the patient, e.g., name, parent's name, telephone number, address, exact diagnosis, and correct dosage. The physician would then designate a specific pharmacy, and the Asellacrin® would be shipped only to that location. This information enabled Serono to determine whether there was a good match between the patient identified in the prescription and a requested shipment.

Serono relied heavily on the PDP program in its marketing efforts. The program was extremely popular among pediatric endocrinologists. Through the PDP program, Serono was able to ensure that Asellacrin® was being made available only to children who had been prescribed the product for its FDA approved use. Thus, there are far less restrictive and costly alternatives than scheduling to control the distribution of hGH.

Another less burdensome approach is education. Serono was the first pharmaceutical company to co-sponsor continuing education programs regarding hGH. Run by the Lawson Wilkins Pediatric Endocrine Society, these programs for doctors covered many aspects of growth disorders. Moreover, the Serono Symposia Division sponsored programs in conjunction with the Human Growth Foundation for children and parents to teach them about hGH. These programs were entirely educational -- there was no product promotion and no marketing activities.

Through these programs, physicians, parents, and patients learned about growth problems and treatment. Serono firmly believes that similar programs could successfully educa athletes and sports physicians regarding the risks of hGH when used in an attempt to improve athletic performance. This approach could adequately address concerns about potential product misuse, without imposing extra burdens upon growth hormone deficient children and their families.

To summarize, based on its extensive familiarity with hGH, Serono is convinced that placing the product in Schedule II would be ill-advised. It is far from clear that hGH misuse constitutes a problem, and even less clear that scheduling the product would affect any misuse that exists. It is clear, however, that scheduling hGH would significantly increase the cost and inconvenience for the patients who need this therapy and their parents. The principal effect of any legislation could very possibly be to cause the greatest burden and hardship to the very children who require hGH for legitimate medical purposes.

STATEMENT OF
NORDISK-USA

Mr. Chairman and Members of the Committee:

I am James L. Smart, President of Nordisk-USA. Nordisk-USA is the American affiliate of Nordisk Gentofte A/S, a Danish pharmaceutical company. Nordisk Gentofte is involved in the research, manufacture and world-wide distribution of insulin, blood plasma products, and other biological and pharmaceutical products. Nordisk Gentofte has under development a recombinant DNA human growth hormone product. Currently it is conducting clinical trials in preparation for submission of a New Drug Application to the Food and Drug Administration ("FDA"). In the future, Nordisk-USA plans to market the recombinant human growth hormone product in the United States. Accordingly, Nordisk-USA is very concerned about this Committee's consideration of legislative proposals which would place human growth hormone products on the list of Schedule II controlled substances. 21 U.S.C. § 812, Pub. L. No. 91-513, 84 Stat. 1247.

Human growth hormone has been approved by FDA as safe and effective for the treatment of severe deficiency of human growth hormone in children. For children suffering from severe deficiencies of human growth hormone, also known as hypopituitary dwarfism, the availability of an artificially produced growth hormone product has meant a continued and sufficient supply of the drug needed to treat their condition. Unfortunately, many believe that because we now possess the ability to manufacture unlimited supplies of human growth hormone, that its potential for abuse or misuse for treating conditions other than hypopituitary dwarfism has increased substantially. Testimony by the members of the panels at this hearing have indicated that misuse is most likely to occur in athletes and normal children whose parents want them to grow taller.

Genentech, Inc. and Eli Lilly and Co. have described the restrictions that their respective companies place on the distribution of their human growth hormone products. Such limited distribution systems are specifically tailored to prevent misuse of human growth hormone. Nordisk intends to structure its distribution system to ensure, to the fullest extent possible, that human growth hormone is made available only to children suffering from diagnosed hypopituitary dwarfism. To that end, Nordisk is willing to distribute the drug directly to the pharmacies of hospitals and clinics with pediatric endocrinology clinics or to pharmacies filling valid prescriptions for human growth hormone and to take such other steps as may be necessary to ensure against diversion of the product for purposes of abuse.

It has been suggested that the appropriate response to the potential for misuse of human growth hormone is to place such compound on the Schedule II list of controlled substances. We respectfully suggest that doing so, would not necessarily curb the potential for misuse of human growth hormone. It may have a detrimental impact on the families of children who need human growth hormone to attain normal height.

Mr. Chairman, it must be remembered that the requirements imposed on Schedule II controlled substances under the Controlled Substances Act and regulations promulgated thereunder are primarily recordkeeping and production requirements. These requirements were designed to enable the Drug Enforcement Administration ("DEA") to track the distribution of drugs with mind-altering and/or dependence-producing pharmacologic activity. The Controlled Substances Act was not, however, intended to serve as a means by which the federal government could regulate the practice of medicine, i.e., the prescribing of approved drugs for indications not listed in their labeling, and the DEA is not particularly well-equipped to take on this task. Thus, while some legislative action may be needed to supplement the measures already taken by the companies to limit distribution of human growth hormone, for a number of reasons placing it on Schedule II of the Controlled Substances Act may not be the most appropriate avenue to take.

First, placing human growth hormone on the Schedule II of controlled substances would increase the recordkeeping requirements of drug companies, physicians, and pharmacies, thereby increasing the cost of the drug to the patients. Moreover, it would mean that prescriptions for human growth hormone could not be refilled routinely by telephone: once human growth hormone became a Schedule II controlled substance, patients receiving human growth hormone would be required to make additional visits to the prescribing physician in order to obtain prescriptions, thereby adding further to the expense of treating hypopituitary dwarfism. Finally, the recordkeeping and production requirements for Schedule II controlled substances would make it more difficult for a small company like Nordisk to place a new human growth hormone product on the market. In addition to obtaining approval from FDA, a company would also have to apply and obtain permission to market the drug from DEA. Also, because production quotas are in place under Schedule II, a company would have to apply for a portion of the quota which first may serve to limit entry into the market and second would keep the price for human growth hormone artificially high. Moreover, there is nothing to guarantee that DEA's decision would be based on the quality of the product produced by our company, vis a vis another. These additional steps would impact most directly on smaller companies, perhaps deterring them from entering the market altogether. While Nordisk recognizes the potential for misuse that exists regarding human growth hormone as a problem that must be addressed, in its opinion, regulation by DEA under the Controlled Substances Act may raise as many problems as it intends to solve.

If the greatest perceived abuse of human growth hormone is in the black market for athletes, then perhaps greater attention should be given to regulating the sale and use of human growth hormone for unapproved uses in athletics. If current law is insufficient to curb such practices as mail order forms for abused substances distributed to athletes, then perhaps steps could be taken to increase the penalties for such practices.

Mr. Chairman, Nordisk intends to cooperate in any meaningful manner to assure that human growth hormone is made available only for its approved use in the most economical manner possible. Nordisk believes it can make a contribution to progress in the treatment of severe growth deficiency in children, and it is for this reason that Nordisk is pursuing the possibility of marketing its human growth hormone product in the U.S.

I appreciate the opportunity to submit these views to the Committee, on behalf of Nordisk-USA.

Respectfully submitted,

Nordisk-USA

0971d

The University of Kansas Medical Center

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April 14, 1987

To: AD HOC Committee on Future
Direction for Synthetic Hormones

From: Dr. Wayne V. Moore, Chairman

With the application of recombinant DNA technology to the production of polypeptide pituitary hormones and with the development of new potent analogs of hypothalamic releasing factor, it is likely that unlimited supplies of potent releasing factors, peptide hormones, and pituitary hormones will be available within the next several years. The competition within the area is also likely to make the cost of these materials relatively inexpensive. This should allow investigators to answer questions that were previously inaccessible due to limited supplies of these hormones. The committee also forsees the possibility of abuse if the development and design of these protocols is not monitored closely. The committee considered each pituitary or hypothalamic hormone separately with regard to potential abuse and use of the hormone.

1) Biosynthetic Human Growth Hormone

The potential abuse of this hormone is widespread treatment of children with short stature conditions in which neither the efficacy nor safety of the growth hormone treatment has been proven. Investigation of the effect of growth hormone in these different conditions will require well controlled multi-center national studies to have sufficient patient population to adequately answer the questions that are being posed. The committee recommends that use of growth hormone in conditions other than growth hormone deficiency and Turner's syndrome be limited to studies that are adequately designed to determine the efficacy of growth hormone in these conditions.

The potential or real abuse of growth hormone by weight lifters and athletes or for "cosmetic" purposes is of such concern that it is being considered as a candidate for Schedule II control.

The intention of preventing the potential or real abuse of growth hormone by athletes as has occurred with anabolic steriods or to prevent attempts to augment the adult heights of children without abnormalities of growth hormone is worthwhile of consideration. The committee suggests that the following points should be considered in this deliberation:

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ADMINISTRATION 588-6301
ALLERGY 588-6300
AMBULATORY SERVICES DIRECTOR 588-5000
[illegible] SCIENCES 588-6316
[illegible] 588-6327

CARDIOLOGY 588-6311
CHAIRPERSON AND DIRECTOR 588-6330
CYSTIC FIBROSIS AND GASTROENTEROLOGY 588-6377

ENDOCRINOLOGY 588-6326
FETAL GROWTH 588-5919
HEMATOLOGY/ONCOLOGY 588-6340
INFECTIOUS DISEASE 588-6336

NEONATOLOGY 588-6337
NEPHROLOGY 588-6323
NEUROLOGY 588-6371
RHEUMATOLOGY 588-6325

1. Statements regarding the real abuse of growth hormone by athletes are unsubstatiated and anecdotal.

2. Statements regarding the positive benefit of hGH to athletes based on the physiological effects of hGH are conjectural and contradicted by conditions of growth hormone excess.

3. The dosage of growth hormone required to enhance the growth promoting and anabolic effects of growth hormone are not known and may be beyond financial or physical possibility.

4. It is possible that the purported supply of biosynthetic growth hormone that is apparently available to athletes may represent counterfeit labels and vials with some inert material in the vial.

5. The proposed controls may not increase the cost of production but they certainly will increase the cost of distribution or prescription.

6. The control of growth hormone would set a precedent that could be applied to future products of recombinant DNA technology.

7. Even though it is difficult or impossible to find a pediatric endocrinologist who has not been "tainted" by association with a pharmaceutical company through the clinical trials of biosynthetic hGH, the deliberations should include input from those physicians that have been and will be most involved in the treatment of children that benefit from growth hormone therapy. This group of physicians is keenly aware of the consequences of limited supplies of growth hormone and most qualified to understand the metabolic consequences of growth hormone.

8. Equal or greater concern should be directed toward black market pituitary growth hormone and other substances being "pushed" as growth hormone. It seems unlikely that the proposed controls on biosynthetic hGH will alter the availability or use of these "growth hormones".

9. The proposed controls must not interfere with research into nonindicated usages of growth hormone and should include provisions to facilitate (administrative and financial) research into the clinical uses of growth hormone including its effect on athletic performance. The committee believes that this approach may be the most productive in preventing or stopping abuse of growth hormone.

The committee recommended support for protocols to study the following:

1) The effect of growth hormone on the growth rate and ultimate adult height of children with nongrowth hormone deficient short stature including intrauterine growth retardation, familial short stature and constitutional delay. This study may require development of techniques for optimal utilization of the growth hormone, and a study of the necessity of continuous administration of growth hormone.

2) Continued study into the use of growth hormone in the treatment of Turner syndrome either alone or in combination with other hormones such as estradiol.

3) Study of the effect of growth hormone on the growth rate and ultimate adult height of children with bone dysplasias. These protocols need to be monitored carefully. The potential for adverse effects may be high in this group of patients since the effects of pharmacological stimulation of abnormal epiphyseal growth centers is not known. For example, the effect of hGH on the size of the foramen magnum in achondroplatic dwarfs would be important to determine.

(cont next page)

4) Studies into the definition, etiology and treatment of children with short stature that might be categorized as having "neurosecretory dysfunction". Efforts should be made to identify and determine the effect of treatment on children who do not have classical growth hormone deficiency as an explanation for their growth failure.

5) The effect of growth hormone on the growth rate and ultimate adult height of patients with craniopharyngioma should be studied further to include a national study on the general management of patients with craniopharyngioma. Questions to be addressed in this protocol could include the effect of craniospinal irradiation on response to growth hormone, the role of radiation and/or surgery in the primary treatment of craniopharyngioma, and new innovative treatment regimens for short stature and growth hormone deficiency associated with craniopharyngioma.

6) Study of the design of the current treatment regimen for growth hormone deficiency with regards to dosage and frequency of administration.

7) Study of other possible uses for growth hormone including wound healing, burns, etc.

8) The development of other routes of GH administration (analogous to nasal and oral insulin).

2) Somatomedin

Since growth hormone deficiency may be considered as a somatomedin C deficiency, the committee recommends that development of biosynthetic somatomedin C be encouraged and that protocols to study the use of somatomedin C as a substitution for growth hormone therapy be encouraged. These studies should be approached with caution since it is possible that direct administration of somatomedin C might bypass some of the control mechanisms that possibly exist with growth hormone and result in non-physiologic somatomedin C levels and attendent untoward side effects. The potential abuse of somatomedin C is similar to that of human growth hormone.

3) LHRH Analog

The committee encourages development of clinical protocols for the use of LHRH analogs in the treatment of precocious puberty, hypogonadotropic hypogonadism, cryptorchidism and possibly constitutional delayed puberty. There does appear to be a potential for abuse of this hormone in the delay of puberty to achieve taller stature.

4) Growth Hormone Releasing Factor

Even though it is recognized that the early studies of the use of growth hormone releasing factor in the treatment of growth hormone deficiency are somewhat discouraging, additional studies into the clinical use of the growth hormone releasing factor should be encouraged. At this point it does not appear that growth hormone releasing factor offers any advantage over the use of growth hormone in the treatment of growth hormone deficiency and there appears to be significant negative aspects to this form of therapy. If a long acting nasal or super agonist form of the growth hormone releasing factor can be developed, the potential clinical usefulness of this hormone may be increased.

Overall, the committee predicts a challenging and exciting future regarding the use of pituitary and hypothalamic hormones. As stated initially, this results from the potential for large quantities of relatively inexpensive hormones that have not been available in the past. This presents the potential for significant, virtual growth in our knowledge in this area, but this growth must be carefully controlled to avoid the ultimate knowledge from becoming acromegalic. Now, more than ever before, we need to encourage a scientific approach to the use of these hormones.

The University of Kansas Medical Center

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May 6, 1987

Dr. Peter Budetti
Subcommittee on Health
and Environment
U.S. House of Representatives
House Bldg A1, Room 512
Washington, D.C. 20515

Dear Dr. Budetti:

The Lawson Wilkins Society met on April 30, 1987 to consider the report of the Committee on the Future Use and Direction of Pituitary Hormones. After considerable discussion, the Society voted to distribute the report to the members for further consideration before finalization of the report. The Society did vote almost unanimously to record its opposition to proposals to make growth hormone a controlled substance. The reason for this opposition is stated in the excerpt (enclosed) of the Committee's preliminary report dealing with the controlled substance issue. The discussion at the Society's meeting indicated that there was approval of the intent of controlling abuse of growth hormone but the proposed means of controlled substance designation does not seem appropriate.

I request that these statements be included as part of the record on the hearings regarding designation of growth hormone as a controlled substance.

Sincerely,

Wayne V. Moore

Wayne V. Moore, M.D., Ph.D.
Professor, Pediatrics
Section of Endocrinology

WVM:jjh

cc: file
Dr. Allan Drash
Dr. Mike Genel
Dr. Gil August

ADMINISTRATION 588 6301
ALLERGY 588 6300
AMBULATORY SERVICES DIRECTOR 588 5900
BEHAVIORAL SCIENCES 588 5716
BUSINESS OFFICE 588 6321

CARDIOLOGY 588 6311
CHAIRPERSON AND DIRECTOR 588 6330
CYSTIC FIBROSIS AND GASTROENTEROLOGY
588 6377

ENDOCRINOLOGY 588 6326
FETAL GROWTH 588 5919
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INFECTIOUS DISEASE 588 6330

NEONATOLOGY 588 6317
NEPHROLOGY 588 6373
NEUROLOGY 588 6371
RHEUMATOLOGY 588 6325

1) Biosynthetic Human Growth Hormone

One potential abuse of this hormone is widespread treatment of children with short stature conditions in which neither the efficacy nor safety of the growth hormone treatment has been proven. Investigation of the effect of growth hormone in these different conditions will require well controlled multi-center national studies to have sufficient patient population to adequately answer the questions that are being posed. The committee recommends that use of growth hormone in conditions other than growth hormone deficiency and Turner's syndrome be limited to studies that are adequately designed to determine the efficacy of growth hormone in these conditions.

Another area of potential or real abuse is the use by athletes and weightlifters to enhance physical performance by increasing strength. Increased surveillance of athletes for use of anabolic steriods may increase the abuse of GH even through its effect on muscle strength is conjectural.

The intention of preventing the potential or real abuse of growth hormone by athletes as has occurred with anabolic steriods or to prevent attempts to augment the adult heights of children without abnormalities of growth hormone is worthwhile of consideration. The committee suggests that the following points should be considered in this deliberation:

1. Statements regarding the real abuse of growth hormone by athletes are unsubstantiated and anecdotal.

2. Statements regarding the positive benefit of hGH to athletes based on the physiological effects of hGH are conjectural and contradicted by conditions of growth hormone excess.

3. The dosage of growth hormone required to enhance the growth promoting and anabolic effects of growth hormone in a non-growth hormone deficient individual is not known and may be beyond financial or physical possibility.

4. It is possible that the purported supply of biosynthetic growth hormone that is apparently available to athletes may represent counterfeit labels and vials with some inert material in the vial.

5. The proposed controls may not increase the cost of production but they certainly will increase the cost of distribution or prescription.

6. The control of growth hormone would set a precedent that could be applied to future products of recombinant DNA technology.

7. Even though it is difficult or impossible to find a Pediatric Endocrinologist who has not been "tainted" by association with a pharmaceutical company through the clinical trials of biosynthetic hGH, the deliberations should include input from those physicians that have been and will be most involved in the treatment of children that benefit from growth hormone therapy. This group of physicians is keenly aware of the consequences of limited supplies of growth hormone and most qualified to understand the metabolic consequences of growth hormone.

8. Equal or greater concern should be directed toward black market pituitary growth hormone and other substances being "pushed" as growth hormone. It seems unlikely that the proposed controls on biosynthetic hGH will alter the availability or use of these "growth hormones".

9. Schedule II status for GH would inhibit and restrict independent research by increasing the paperwork required to initiate and use GH for nonindicated uses and by eliminating the ability of the drug companies to distribute free hormone.

10. Schedule II status would eliminate the current practice of the drug companies of underwriting therapy for children without any means of payment.

11. The proposed controls must not interfere with research into nonindicated usages of growth hormone and should include provisions to facilitate (administratively and financially) research into the clinical uses of growth hormone including its effect on athletic performance. The committee believes that this approach may be the most productive in preventing or stopping abuse of growth hormone.

PUBLIC POLICY COUNCIL

of the

American Pediatric Society
Charles Alford, Jr., M.D.
University of Alabama
Myron Genel, M.D.
Yale University

Association of Medical School Pediatric Department Chairmen
Robert Blizzard, M.D.
University of Virginia
Thomas K. Oliver, Jr., M.D.
University of Pittsburgh

Society for Pediatric Research
William F. Balistreri, M.D.
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Reply to:
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Box 3333
New Haven, Connecticut 06510
(203) 785-6019
Chairman

April 9, 1987

Wayne V. Moore, M.D., Ph.D.
Chairman, Committee on Future Uses
of Synthetic Hormones
Lawson Wilkins Pediatric Endocrine Society
Dept. Pediatrics
University of Kansas Medical Center
Rainbow Blvd. at 39th Street
Kansas City, Kansas 66103

Dear Wayne:

Per our conversation today, attached is a summary and testimonies from the hearing yesterday on the abuses of human growth hormone. I would encourage you to follow through with discussions with Dr. Budetti of Rep. Waxman's staff to explore the possibility of the inclusion of your committee's reports and other discussion from the upcoming business meeting in the hearing record for yesterday.

I believe we agree it is appropriate for the society to be engaged in discussions about possible legislative proposals which would affect the distribution and use of synthetic human growth hormone.

Sincerely,

Myron Genel, M.D.

cc: Sam Raiti, M.D.
Claude Migeon, M.D.
Peter Budetti, M.D.

Members of: Council of Academic Societies, Association of American Medical Colleges
Council on Government Affairs, American Academy of Pediatrics

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April 13, 1987

Congressman Henry Waxman
Chairman, Health and Environment Subcommittee
Committee on Energy and Commerce
U. S. House of Representatives
Washington, D.C. 20515

Dear Sir:

Please include this letter as a component of the record for the hearing held April 8, 1987, regarding possible regulation of human growth hormone as a class II controlled substance.

My qualifications for expressing a knowledgeable opinion regarding this proposal are as follows:

(1) Pediatric endocrinologist for 30 years.
(2) One of very first endocrinologists to administer human growth hormone (1959).
(3) Appointed as first Director of National Pituitary Agency by United States Department of Health and Welfare (1961).
(4) Continued as advisor to Agency until 1985.
(5) Served as consultant to National Institute of Health (1960-present) - particularly in field of growth.
(6) Past president of Human Growth Foundation.
(7) Physician to over 1,000 growth hormone deficient patients (1957-present) and over 5,000 children with other causes of short stature.
(8) Investigator having administered human growth hormone to approximately 1,000 individuals since 1959.

The concerns registered in this letter are those which I personally have, although held in common with many other endocrinologists. The expression of those concerns is not to be interpreted as my acting as spokesman for any scientific society or for industry, although I suspect many responsible physicians would appreciate my expressing these concerns also on their behalf.

I do have concerns that there is the potential for human growth hormone to be abused and/or misused, as there is the potential for vitamins, antibiotics, analgesics, and hormones other than growth hormone to be misused and abused. Although human growth hormone may be misused, it will not be abused unless it is given in unusually large or pharmacologic amounts, as the usual therapeutic or physiologic amounts of growth hormone have not been demonstrated to be injurious. In this respect human

Office of the Chairman

growth hormone is analogous to thyroid hormone, cortisone, testosterone, estrogen and vitamins.

The potential abusers of growth hormone fall into two categories.

(1) Athletes who wish to enhance their prowess by developing muscle mass.
(2) Normally statured children who are enticed or coerced by their parents to receive pharmacologic doses of growth hormone, in the hope that the child will achieve a height which is above his expected height, even though the expected height falls in the normal range.

The potential misuse of growth hormone may fall into several categories.

(1) The administration of growth hormone to non-growth hormone deficient children who are markedly short and who hope to grow as a consequence of receiving growth hormone.
(2) The administration of growth hormone to elderly individuals who hope to deter the ravages of aging.
(3) The administration of growth homrone to minimize and/or treat obesity.

Since investigators soon will have the answers regarding the possible effective use of growth hormone in non-growth hormone deficient short children, in slowing the aging process, and in the treatment of obesity, legislators should not focus their attention on the possible misuse but on the potential abuse of hormone.

Some athletes and a few misdirected parents will attempt to divert growth hormone from the legitimate market. They may occasionally be successful in certain instances regardless of the regulations and threatened penalties. For example, such regulations and threatened penalties have not prevented active use of narcotics, stimulants, or steroids by athletes.

Theoretically the enactment of regulations through drug enforcement agencies might be effective in deterring such abuse. However, legislators must ask whether the thwarting of abuse by a few athletes and a few misdirected parents justifies:

(1) the cost of time, effort and dollars to physicians and drug enforcement agencies
(2) the limitations of hormone to patients who need same because of consequent increased costs and/or resultant limitations of supply

Legislators also must ask if it is their responsibility to protect athletes or a few normal children from their parents when the "toxicity" that is a matter of concern with abuse occurs only with long term exposure to pharmacologic amounts of growth hormone. Toxicity has been observed only in patients with tumors producing pharmacologic amounts of growth hormone over several years.

The adverse consequences which would occur by passing legislation classifying growth hormone as a class II controlled substance, in my opinion, are the following, and I preface these statements by stating that they are concerns of mine as a physician and not prompted by the statements or concerns of commercial companies.

(1) Drug enforcement agencies will spend valuable time, effort and dollars, all of which are currently limited and inadequate for these agencies to adequately police life threatening controlled drugs such as morphine, amphetamines, etc., which it is now their responsibility to police. This would be a misdirection of resources.
(2) Patients who need growth hormone might not have this available to them because of the limited amounts that would be manufactured and distributed under the regulations governing "controlled substances".
(3) The costs of growth hormone will remain greater than desirable, which will prevent needy patients from receiving the hormone and/or inappropriately increase the costs of health care to all of us because of costly insurance premiums.
(4) The currently controlled distribution process, as established by reputable pharmaceutical firms (Eli Lilly, Genentech) will be torn asunder, and with the availability of hormone in small local pharmacies, the opportunity for abuse will be increased over the very limited opportunity currently existing.

As I wrote to Dr. Peter Budetti, your counsel and aid, on October 29, 1986, I plead that education be the mechanism that we use to deter the possible abuse and misuse of biosynthetic growth hormone instead of legislation. In my opinion, legislation which has neither been proven to be needed, or which may be more detrimental than beneficial, should not be proposed. Historically, a program once initiated by legislation, good or poor, is with us for decades. On behalf of those who will receive growth hormone for good cause, I urge that you defer proposing legislation to make growth hormone a controlled substance until significant abuse with toxicity is demonstrated, and/or until such time that there is reasonable chance that the legislation is more beneficial than detrimental to those the legislators are trying to protect.

Respectfully submitted,

Robert M. Blizzard, M.D.
Director, Children's Medical
Center

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May 12, 1987

Congressman Henry Waxman
Chairman, Health & Environment Subcommittee
Committee on Energy and Commerce
U..S. House of Representatives
Washington, D.C. 20515

Dear Congressman Waxman:

This is in reply to your letter of May 6, 1987.

I reiterate that the concerns raised are mine as a physician and are not prompted by the statements or concerns of commercial companies. This statement was made in my letter to you of April 13, 1987, in which I stated, "The expression of these concerns is not to be interpreted as my acting as spokesman for any scientific society or for industry ... etc."

My concerns were expressed in my initial letter to you and are re-expressed now because I am first and foremost an advocate for children as I understand that you are also. My advocacy for children ties in with my profession of pediatrics. My advocacy for children is why I was a founder of the Human Growth Foundation and why I have attempted to assist children to grow who are dwarfed. I wrote on behalf of children and their parents and not on behalf of industry.

My qualifications for expressing a knowledgeable opinion regarding the proposal under consideration are those listed in my letter of April 13th. Those qualifications also are those which permitted me to undertake the establishment of a newsletter, Growth, Genetics, and Hormones, which is supported under an educational grant from Genentech. The purpose of this journal is to bring to pediatricians and geneticists current reviews of the literature on nutritional problems, genetic problems, and growth problems. As part of these reviews, one will note that more than 50% of the articles and the abstracts reviewed concern problems totally unrelated to growth hormone. I have included several issues for your review to confirm that that is correct.

Office of the Chairman

I would like to call your attention to the Letter from the Editor in Vol. 1, #4 (page 5). Please note that in the last paragraph I state, "physicians providing medical care to children should make every effort to identify - and provide proper evaluation and treatment for - growth hormone deficient children. However, as a pediatric endocrinologist with many years of experience, I am concerned that this hormone may be abused and given indiscriminately to children who may or may not benefit from it. Hopefully physicians will resist the pressures to prescribe growth hormone for children who have not been adequately diagnosed as growth hormone deficient". I present this statement to you to emphasize my belief that growth hormone must be used judiciously and not misused or abused, and also to emphasize my belief that education is the mechanism which we should use to prevent misuse and abuse. Growth, Genetics, and Hormones is used for that purpose.

I would like to emphasize that the editorial board at its first meeting stated unequivocally, and it is recorded in the minutes, that the board would be an independent body which would act completely upon its own without any interference or action by, and without any obligation to, Genentech, Inc. The editorial board has rigidly followed this policy. I do receive remuneration for my time spent as an editor and these funds come from the educational grant.

In your letter to me of May 6, 1987, you request that I identify any relationship between myself and any company producing growth hormone. I have been sought out by Genentech, Inc., Eli Lilly Corp, and Serono, Inc., as might be expected from my credentials, for advice and to participate in educational conferences. It is my obligation as a scientist and a man with much experience to assist industry in promoting educational efforts which will prevent the misuse or abuse of synthesized products. In such a role I have periodically been appropriately paid as a lecturer or as a consultant for the time invested. As such a lecturer and consultant I have frequently discouraged misuse and abuse and misrepresentation.

Through my 30 years of scientific investigation I have tested the therapeutic and toxic effects of many hormones. Such studies have been undertaken with financial support for these studies being supplied by various drug companies. During these years I

Congressman Waxman
May 12, 1987
Page Three

have published many articles indicating that the therapeutic agents under testing were ineffective. When the agents have proven to be effective I have published these facts. The same applies for studies with human growth hormone. Monies received have been for the care of patients and not for professional or personal recompense to me.

I trust that as an intelligent person responsible for seeing that the best health care is delivered to citizens of this country that you would want the research done by the best individuals possible, and that you would expect that this research would be financed by the institutions - financial or governmental - which are trying to obtain appropriate answers. This is the manner in which I have functioned and performed.

In your letter to me of May 6, 1987, you suggest that I review the entire transcript of the hearing when it is published, since much of the testimony bears on and runs somewhat counter to the points I raised. I am certain that some of the testimony is counter to the points which I raised. However, I am also certain that legislation at this time will be counter productive and will not accomplish the goals which we all wish to accomplish. If the goals are accomplished, it will be at tremendous expense and effort to not only patients and physicians, but also to drug enforcement agencies.

I would like to thank you for your efforts as the Chairman of the Subcommitee on Health and Environment. You have been a wise counselor and legislator for many activities of children. I am trusting that you and your committee will act similarly in respect to the contemplated legislation in this instance. In the event that education and other measures do not prevent significant abuse of growth hormone, legislation of the type which you are suggesting can be passed in one, two or three years from now. Growth hormone is not addictive, and there is no evidence that it is significantly adverse in its physiological action if given over a two or three year period. Growth hormone should not be considered along with cocaine and marijuana. It is an effective therapeutic agent.

I am requesting that this entire letter be incorporated into the substance of the remarks that you intend to place in the record to give proper perspective to the record. To abstract any part of these statements from this letter without incorporating the full letter would not only be unfair but would not supply the complete and comprehensive information which you undoubtedly wish to supply to the members of your distinguished committee.

Respectfully submitted,

Robert M. Blizzard, M.D.
Director, Children's Medical
Center

MEDICAL DEVICES AND DRUG ISSUES
Prescription Drug Price Increases

TUESDAY, APRIL 21, 1987

House of Representatives,
Committee on Energy and Commerce,
Subcommittee on Health and the Environment,
Washington, DC.

The subcommittee met, pursuant to notice, at 9:52 a.m., in room 2123, Rayburn House Office Building, the Hon. Henry A. Waxman (chairman) presiding.

Mr. Waxman. The meeting of the subcommittee will come to order. The purpose of today's hearing is to investigate the dramatic and continuing price increases for prescription drugs. In particular, we want to explore whether the reasons cited by the drug industry for these price increases have any basis in fact.

As many of you know, this subcommittee held hearings in July 1985 to examine prescription drug price increases. At that time, prices were increasing at a rate roughly twice that of the Consumer Price Index. Also at that time, witnesses for the drug industry told us that increases of that magnitude were only a temporary phenomenon. As it turns out, they were right. Today, drug prices outstrip the CPI by far more than they did then. Since July 1985, the CPI has risen by 2.7 percent. Prescription drug prices have risen 12.2 percent; a record 4.5 times greater than the Consumer Price Index.

As we stated at the last hearing, unless the industry can provide an adequate explanation for these price hikes, one can only conclude that what is going on is greed on a massive scale.

This hearing is to determine whether the industry has an explanation for its price increases. At the outset, I must say I'm terribly skeptical. I gather that the rationale offered at our last hearing will be the same we will hear this year, namely price increases are essential if research and development is to be expanded.

This is a rationale that we now have investigated thoroughly. As part of the preparation for this hearing, the subcommittee surveyed the 25 largest pharmaceutical manufacturers constituting roughly ⅔ of the industry by sales, to determine whether their price increases were necessary to pay for their increases in research and development. The results are summarized in the staff report issued today and they are not encouraging.

Based on data supplied by these manufacturers to the subcommittee, it's clear that the pharmaceutical industry has misled the American people. Most of the money generated by the recent enormous price increases is not going to fund R&D. Between the years 1982 and 1986, drug price increases produced revenue gains of $4.7 billion. During the same period, research and development expenditures rose only $1.6 billion or about ⅓ of the revenue gains from price increases.

In short, the money was arriving in bucket loads but going to R&D in spoonfuls.

We need to know what is going on with the drug industry. Too many Americans depend on life-saving drugs for Congress to let prices skyrocket without a clear explanation from the companies involved. We must constantly remember that most Americans get drugs only one way: by paying for them out of their own pockets. Only a small fraction of the drugs consumed in the United States gets paid for by the Government or by health insurance.

This particularly affects the elderly, most of whom live on fixed incomes. While they constitute 11 percent of the population in this country, they consume roughly 30 percent of the drugs prescribed each year. As we will hear today, the elderly are upset and concerned about the prices they pay for drugs.

As we begin the hearing, let me repeat a key point. We focus these hearings on the pharmaceutical industry not in spite of the enormous benefits of its products but because of these benefits. Drugs are important to our health. We must guarantee they are denied to no one simply because they cost too much.

Before calling on our witnesses, I want to recognize members of the subcommittee for opening statements they wish to make and first of all, I want to call on a distinguished member of our subcommittee, Congressman Whittaker, for any comments he wishes to make.

Mr. WHITTAKER. Thank you, Mr. Chairman.

This morning we resume an inquiry that this subcommittee began nearly 2 years ago. At issue is whether the traditional market forces protect the consumer of prescription drugs while at the same time allowing viability of the drugs' manufacturers. We heard disagreement on this issue in July of 1985 and I fully expect we will again this morning.

I am sympathetic with the plight of the elderly patients, whose prescriptions are expensive and not covered by his or her health insurance plan. Prescription drugs are not discretionary items that can be foregone one month because one's resources do not allow their purchase.

I also think that the pharmaceutical industry has a responsibility which in the most part it has met, to develop the most up to date products to protect our health. The industry must finance this obligation through the prices of charges. I recognize that patent protection may give a pharmaceutical company the opportunity to charge a price higher than could be charged if there were a competing product.

This country has had a long tradition of providing incentives for the development of new products through patent protections. I sincerely hope we assess the repercussions of modifying those protections before we even think about changing them.

I request that each of the witnesses keep in mind that the members of this subcommittee are very interested to know how the abbreviated new drug application patent term restoration and drug export laws that were passed in 1984 and 1986 have affected domestic drug pricing.

Thank you, Mr. Chairman.

Mr. **Waxman.** Thank you, Mr. Whittaker. Mr. Sikorski.

Mr. **Sikorski.** I have no statement, Mr. Chairman, other than I do commend you and the staff for moving this discussion forward.

Mr. **Waxman.** Thank you very much. Mr. Wyden.

Mr. **Wyden.** Thank you, Mr. Chairman. I, too, think these are very important hearings and it seems clear to me drug prices are going up at an exceptionally high level. The question is why. When you listen to people in the industry, they will say that it is Government policies feeding these huge price increases. On the other side, when you listen to people in Government, it seems the practices in the private sector are the ones that are contributing to these very high increases.

I think what we need to do today is to look at what is really contributing to these increases and figure out what can be done about it.

For example, I would like to know exactly what it means when industry representatives say that $4.6 billion was spent on R&D in 1986. How much of that was on initial research in the new therapies? How much on clinical trials? How much on research to submit to the Food and Drug Administration? How much on marketing and market research?

It just seems to me, Mr. Chairman, that we are in the dark with respect to the key issues that go into drug pricing. I want to see us keep this work in the marketplace but my understanding is that marketplace forces don't come into play much in the drug industry.

I think to really get to the heart of this problem, we are going to have to start getting some basic information. We are going to have to shed some light on the key issues that relate to drug pricing. These hearings give us that chance, Mr. Chairman. I appreciate your going forward with this session.

Mr. **Waxman.** Thank you very much, Mr. Wyden.

We have prepared to be distributed today a second Staff Report on price increases for prescription drugs and related information. It is dated April 21, 1987. By unanimous consent, I would like to have that Staff Report inserted in the record. Without objection, that will be the order.

[Testimony resumes on p. 215.]

[The staff report follows:]

SECOND STAFF REPORT
ON
PRICE INCREASES FOR PRESCRIPTION DRUGS
AND RELATED INFORMATION

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The information contained in this report has been compiled by the staff of the Subcommittee on Health and the Environment.

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SUMMARY OF FINDINGS

SECOND STAFF REPORT ON PRICE INCREASES FOR PRESCRIPTION DRUGS AND RELATED INFORMATION

SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT
APRIL 21, 1987

Background: In July, 1985, the Subcommittee on Health and the Environment conducted its first hearing to explore the unprecedented price increases for prescription drugs that began in 1981. Prior to 1981, prescription drug price increases had outpaced the consumer price index only one time since 1967. From January, 1981 through June, 1985, the CPI rose 23% while prescription drug prices rose 56%.

At the 1985 hearing, pharmaceutical industry witnesses testified that the high price increases since 1981 were temporary fluctuations from their normal pattern. They claimed that the increases were essential if drug companies were to raise their expenditures for research and development of new drugs.

Industry Trends: Price increases since July, 1985 have continued at record high levels. The CPI has risen 2.7% since July 1, 1985, while retail prescription drug prices have risen 12.2% -- a record 4 1/2 times greater. When compared to the period beginning January, 1981, the CPI rose 28% through December, 1986, while prescription drug prices rose over 79%.

Companies Invited to 1987 Hearings: The ten companies invited to testify at the Subcommittee's April 21, 1987 hearing have price increases that are typical of the entire industry. These companies also have many of the top-selling drugs. Set forth below are examples of price increases for 1986 from the six companies invited to testify who have declined to appear at the hearing:

Company	Drug and Ranking	1986 Average Wholesale Price Increase
American Home Products	Inderal (28)	19%
Burroughs Wellcome	Lanoxin (4)	50%
Glaxo	Zantac (8)	14%
Eli Lilly	Darvocet-N (5)	10%
Hoffmann-La Roche	Valium (9)	19%
SmithKline Beckman	Tagamet (3)	21%

(See Tables 6 and 7)

Source: IMS, Ltd.
Medi-Span

Subcommittee Survey: In order to evaluate the drug industry's continuing claim that substantial price increases are required in order to raise research and development expenditures, the Subcommittee surveyed the twenty-five largest companies (by prescription drug sales volume) in the Pharmaceutical Manufacturers Association. The twenty-four responding companies constitute two-thirds of all prescription drug sales in the U.S.

Data submitted by the companies and aggregated in this report indicate that the industry has misrepresented the facts. Between 1982 and 1986, drug price increases produced revenue gains of $4.7 billion while research and development expenditures rose $1.6 billion. Price rises produced three times the revenue needed to fund every dollar of new research and development. In addition to the revenues generated from price increases, the same companies had an additional $4.2 billion of increased revenues. During this five year period, the companies increased their total revenues by $8.9 billion while increasing their research and development expenditures by $1.6 billion. (See Tables 1-3).

During this same five year period, the companies raised their marketing and detailing expenditures by almost the same amount -- $1.4 billion. (See Table 1).

Generic Drugs Cheaper; Prices Going Down: In the face of extremely high price increases for brand name prescription drugs, consumers currently have only one option. For off-patent brand name drugs, like Inderal and Darvocet-N, consumers can purchase generic versions at significantly lower prices. In addition, generic prices are declining at the same time brand name drug prices are rising. (See Tables 10-12).

Economics of Pharmaceutical Industry Unusual: Pharmaceutical companies claim that the industry is intensely competitive. Clearly, companies do compete to find the next major breakthrough drug. However, whatever competition there is does not affect companies' ability to raise prices.

During the time that drugs are under patent, companies have raised prices constantly. In addition, through advertising to doctors, consumer "loyalty" developed during the period the drug is patented and deliberate efforts to discourage generic use, brand name drug companies have created an economic marketplace that allows them to raise prices even after patents expire and generics can compete.

EXPLANATION AND MAJOR FINDINGS OF SURVEY CONDUCTED BY SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT

Explanation

The Subcommittee on Health and the Environment recently completed a survey of the twenty-five largest (by sales volumes of prescription drugs) pharmaceutical companies in the Pharmaceutical Manufacturers Association. The letter and questionnaire are included in attachment I. The questionnaire defined the terms "research and development" and "marketing and detailing".

Twenty-four companies responded to the questionnaire in a manner that allowed the results to be aggregated. Revenues of the twenty-four companies make up two-thirds of all prescription drug sales in the United States.

Major Findings

1. Increases in revenues from price changes are significantly larger than increases in R and D expenditures during the period 1982-1986. Companies raised their prices far more than was necessary to pay for all increases in R and D expenditures.

Between 1982 and 1986, drug price increases produced revenue gains of $4.738 billion while R and D expenditures rose $1.632 billion. The revenue gains were 290% larger than the total increase in R and D expenditures. In the years 1982-1986, drug price related revenue increases were from 240% to 380% larger than the total increases in R and D expenditures for those years.

2. Total revenue increases are almost twice as large as the revenues derived from price increases.

Revenue increases can result from actions other than raising prices. For example, new drugs can be introduced and the volume of sales of marketed drugs can increase. Total revenue increases from non-price related actions during the period 1982-1986 provided substantial additional revenues.

Between 1982 and 1986, non-price related increases were $4.168 billion while R and D expenditures rose $1.632 billion.

3. Twenty-two of the twenty-four responding companies had increases in revenues from price changes that were greater than increases in expenditures for R and D for the period 1982-1986.

All responding companies were grouped according to the percentage by which their increases in revenues due to price increases during the five years 1982-1986 exceeded their increases in R and D expenditures during the same period. Two companies raised R and D more than the price-related revenues they received. Twenty-two of twenty-four had greater revenues. Eight of 24 had price-related revenues that were 4 to 10 times greater than R and D expenditure increases.

4. Marketing and Detailing expenditures were greater than R and D expenditures during the period 1982-1986.

In total dollars and as a percentage of sales, the 23 companies providing data spent more on marketing and detailing than on R and D during the years 1982-1986. In 1985 and 1986, total R and D exceeded total marketing and detailing by a small amount.

These data raise the question of whether recent price increases were to raise revenues for higher expenditures for marketing and detailing as much as for R and D.

5. For the same drugs, prices in the U.S. are consistently higher than in foreign countries.

Because confidential data were used, the Subcommittee cannot release actual prices. The U.S. and foreign prices of 130 drugs were supplied to the Subcommittee. Counting each foreign country in which those drugs were sold, the U.S. price exceeded the foreign price 79% of the time (288 times), while the foreign price was greater 21% of the time (76 times).

6. Generic drugs are made by many "brand name" or research-oriented companies.

Thirteen of the 25 responding companies make generic drugs either in a subsidiary or in the company itself.

SUMMARY OF TABLES

Table 1: These data provide a comparison of revenues, revenue increases from price increases, R and D expenditures and marketing and detailing expenditures for each year 1982-1986 and for all five years in aggregate. (See Explanation and Major Findings of Survey above.)

Table 1A: These data group companies according to the percent by which their increases in revenues due to price changes exceed their increases in R and D expenditures for each year 1982-1986 and for all five years in aggregate. (See Explanation and Major Findings of Survey above.)

Table 2: These data compare R and D expenditures and marketing and detailing expenditures for each year 1982-1986 and for all five years in aggregate. (See Explanation and Major Findings of Survey above.)

Table 3: These data indicate that a large number of research-oriented companies also make one or more generic drugs.

Table 4 and Accompanying Chart: These data demonstrate that following a number of years (roughly 1968-1980) in which the CPI rose at a higher rate than the retail price of prescription drugs, the situation suddenly reversed and, for the past five years, prescription drug prices have grown dramatically faster than the CPI. At the time of the Subcommittee's hearing in July, 1985, prices were growing at a rate two to three times as fast as the CPI. Since the hearing, the CPI has risen 2.7% while prescription drug prices have risen 12.2% -- a record 4 1/2 times greater.

Table 5 and Accompanying Chart: These data compare the CPI and the producer prices of prescription drugs for the same period as Table 4 and its accompanying chart. These data indicate that the increase in prices to consumers has resulted from increases at the manufacturer rather than the retailer level.

Table 6: These data show the wholesale price increases for the top 20 selling drugs in the United States. In virtually every instance, the prices of these drugs have risen substantially faster than the CPI during the same period. For example, during the period from January 1, 1981 to December 31, 1986, the CPI rose 28%. During the same period, the price of Dyazide rose 88% while the price of Lanoxin .125 rose 526%.

Table 7: These data provide percentage price increases for 1985 and 1986 for the best-selling products of the ten companies invited to testify before the Subcommittee on Health and the Environment on April 21, 1987. Increases for most products are far greater than the increase in the CPI.

Table 8: This table lists the top twenty selling drugs for all sizes and dosages in the United States by sales volume (retail plus hospitals).

Table 9: This table compares profit data for all manufacturers versus pharmaceutical manufacturers in two ways: (i) profits per dollar of sales, after taxes and (ii) annual rates of profit on shareholder's equity, after taxes.

Pharmaceutical manufacturers have consistently maintained higher profit rates than other manufacturers in the United States. Because of the relatively inelastic demand for most drugs and certain market conditions (e.g., the ability to control prices for patented drugs), pharmaceutical manufactures generally are able to maintain or increase sales even when raising prices.

The level of profits per sales dollar indicates that while the drug manufacturers claim that they have raised prices to finance R and D in recent years, they also have substantially increased the percentage of every sales dollar which is profit.

Table 10: This table compares for the years 1984-86 the prices charged by brand name and generic manufacturers for prescription drugs. In most instances, the price of the generic equivalent started at a point lower than the brand name and fell while the price of the brand name drug started at a higher level and increased.

Table 11: This table, derived from information submitted by REVCO, a large drug store chain, shows price trends for selected top-selling brand name prescription drugs and their generic equivalents. During the period when generic prices were falling dramatically, prices for brand name drugs rose significantly.

Table 12: This table, derived from data submitted by the American Association of Retired Persons Pharmacy Service, the largest mail order pharmacy service in the United States, compares the prices the pharmacy service charged for brand name drugs and their generic equivalents. In all instance, the generic equivalent cost substantially less than the brand name drug.

TABLE 1

RESULTS OF SURVEY BY THE SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT: MAJOR FINDINGS

	1982*	1983	1984	1985	1986	Total
			(in millions)			
Total Revenues from prescription drugs	9,881.5	11,548.4	12,318.9	14,434.7	16,583.1	64,721.6
Increase in revenues over previous year	2,343.8	1,528.4	770.5	2,115.8	2,148.4	8,906.9
Amount of revenue increases from price changes	976.1	940.5	818.1	959.6	1,043.9	4,738.2
Increase in R & D expenditures over previous year**	256.4	284.3	344.7	348.1	398.8	1,632.3
Increase in Marketing and Detailing expenditures over previous year***	364.5	274.7	205.6	250.2	307.5	1,402.5
Percent by which increases in total revenues exceed increases in R & D	914%	540%	220%	610%	540%	546%
Percent by which increases in revenues from price changes exceed increases in R & D expenditures	380%	330%	240%	280%	260%	290%

TABLE 1 (con't)

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* The 1982 figures are based on reports from 23 companies because one of the 24 companies responding to the survey did not provide its "revenue increases due to price changes." (The company did provide its 1982 total revenues and its 1982 R and D expenditures.) All other years reflect reports based on 24 companies.

** Research and Development (R and D) expenditures for a year are calculated by reducing total R and D expenditures for the year by the amount of tax credits that were taken in that year for R and D expenditures. (The tax laws allow a pharmaceutical company to take a credit against its taxes in an amount equal to a portion of the company's increase in its R and D expenditures.)

*** Because not all companies reported fully, expenditures for Marketing and Detailing are slightly understated. Expenditures for 1982 are based on reports from 22 companies. Expenditures for 1983-86 are based on reports from 23 companies.

TABLE 1A

RESULTS OF SURVEY BY SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT: REVENUE INCREASES FROM PRICE CHANGES VERSUS R & D INCREASES

Explanation: This chart groups companies according to the percentage by which their increases in revenues due to price changes exceed their increases in R and D expenditures. The grouping is provided for each of five years and for the average of the five years. One of the 24 responding companies did not provide sufficient data for 1982. That company's average is based on four years of data.

Percentage Category*	Number of Companies with five year average percent in category	Number of Companies with annual percentage in category				
		1982	1983	1984	1985	1986
<100%	2	2	2	4	4	5
101%-200%	5	3	8	7	3	4
201%-400%	9	9	7	8	10	6
401%-600%	5	2	4	3	3	2
601%-1000%	2	5	1	0	2	4
>1000%	1	2	2	2	2	3

---

* The "percentage category" is calculated by dividing the increase in revenues due to price changes by the increase in R and D expenditures. If the increase in revenues is greater than the increase in R and D, the percent will be 101% or larger. If the increase in revenues is less than the increase in R and d, the percent will be less than 100%.

TABLE 2

RESULTS OF SURVEY BY THE SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT: R & D EXPENDITURES VERSUS MARKETING AND DETAILING EXPENDITURES*

	1982	1983	1984	1985	1986	Total
		(in millions)				
Total Revenues from prescription drugs	9,981.5	11,497.5	12,118.4	14,078.4	15,963.5	63,639.3
Total R&D expenditures**	1,846.3	2,130.1	2,472.2	2,816.6	3,213.4	12,478.5
Total marketing and detailing expenditures	2,066.4	2,341.1	2,546.7	2,796.9	3,104.4	12,855.5
R & D expenditures as % of sales	18.5%	18.5%	20.4%	20.0%	20.1%	19.6%
Marketing and detailing expenditures as % of sales	20.7%	20.4%	21.0%	19.9%	19.4%	20.2%

---

* This chart is based on reports from 23 companies.

** Research and Development (R and D) expenditures for a year are calculated by reducing total R and D expenditures for the year by the amount of tax credits that were taken in that year for R and D expenditures. (The tax laws allow a pharmaceutical company to take a credit against its taxes in an amount equal to a portion of the company's increase in its R and D expenditures.)

TABLE 3

RESULTS OF SURVEY BY SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT: GENERIC DRUGS AND MAJOR BRAND NAME COMPANIES

Explanation: The survey respondents were asked whether they make generic drugs either in their corporation or in a subsidiary. The responses were categorized as follows.

Category	Number of Companies
Do not make in company or in subsidiary	12
Make in company	8
Make in subsidiary	5

TABLE 4

COMPARISON OF PRICE CHANGES: CPI VERSUS RETAIL PRESCRIPTION DRUGS

	Consumer Price Index (% Price change)	Prescription Drugs (Retail) (% Price change)
1967	----	----
1968	4.2	-1.7
1969	5.4	1.3
1970	5.9	1.6
1971	4.3	.1
1972	3.3	-.4
1973	6.2	-.4
1974	11.0	2.4
1975	9.1	6.2
1976	5.8	5.4
1977	6.5	6.0
1978	7.7	7.8
1979	11.3	7.8
1980	13.5	9.2
1981	10.4	11.4
1982	6.1	11.7
1983	3.2	10.9
1984	4.3	9.6
1985	3.6	9.5
1986	1.9	8.6

Source: Bureau of Labor Statistics

Comparison of Price Changes: CPI versus Retail Prescription Drugs

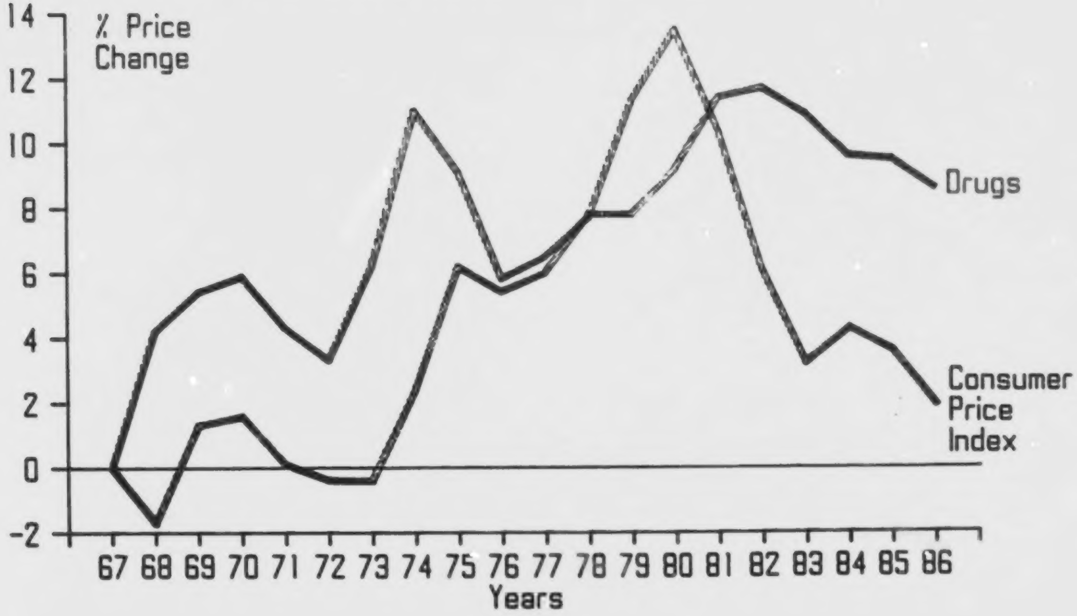

TABLE 5

COMPARISON OF PRICE CHANGES: CPI VERSUS PRESCRIPTION DRUGS (PRODUCER PRICES)

	Consumer Price Index (% Price Change)	Prescription Drugs (Producer Prices) (% Price Change)
1967	----	----
1968	4.2	-1.0
1969	5.4	.5
1970	5.9	-.2
1971	4.3	-.3
1972	3.3	.1
1973	6.2	.8
1974	11.0	4.3
1975	9.1	8.6
1976	5.8	6.3
1977	6.5	4.2
1978	7.7	5.2
1979	11.3	7.0
1980	13.5	8.8
1981	10.4	11.7
1982	6.1	11.1
1983	3.2	10.7
1984	4.3	9.3
1985	3.6	9.2
1986	1.9	8.7

Source: Bureau of Labor Statistics

Comparison of Price Changes: CPI versus Prescription Drugs (Producer Prices)

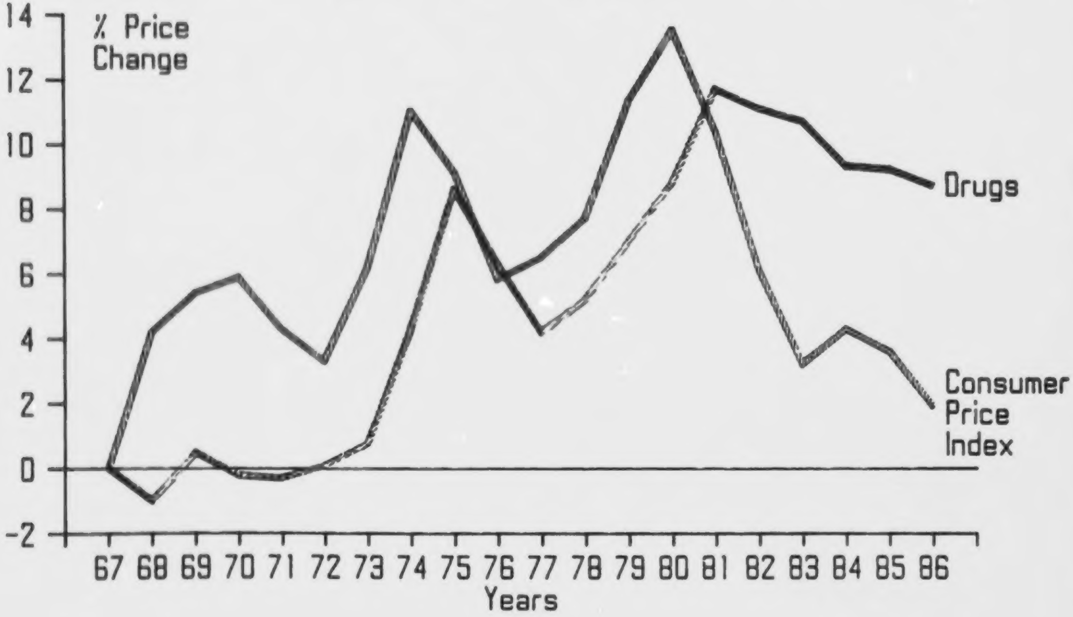

TABLE 6

PERCENTAGE PRICE INCREASES FOR THE TWENTY TOP-SELLING U.S. PRESCRIPTION DRUGS (AVERAGE WHOLESALE PRICE)

	Company	Drug*	1981	1982	1983	1984	1985	1986
1.	SmithKline Beckman	Dyazide (caps)	8.2	10.1	12.2	23.5	12.1	10.1
2.	Johnson & Johnson	Tylenol #3	0.0	0.0	5.4	4.9	0.0	18.6
3.	SmithKline Beckman	Tagamet (300mg)	6.2	14.0	0.0	12.0	9.9	21.0
4.	Burroughs Wellcome	Lanoxin (.25mg)	32.8	19.9	25.6	43.6	33.7	50.0
5.	Eli Lilly	Darvocet-N(100mg)	15.0	15.0	12.0	19.9	9.0	9.9
6.	Burroughs Wellcome	Lanoxin (.125mg)	33.0	20.3	24.4	49.3	40.3	50.0
7.	ICI (Stuart Pharmaceuticals)	Tenormin (50mg)	0.0	12.0	4.0	9.0	14.4	8.2
8.	Glaxo	Zantac (150mg)	NFDA	NFDA	AFDA	7.9	9.9	14.8
9.	Hoffmann-La Roche	Valium (5mg)	3.5	10.8	20.0	20.0	9.6	19.3
10.	Ciba-Geigy	Slow K (600mg)	0.0	9.9	7.0	4.9	5.1	4.9
11.	Hoechst Roussel	Lasix (40mg)	0.0	10.2	0.0	0.0	0.0	0.0
12.	Pfizer	Procardia (10mg)	AFDA	0.0	9.0	9.7	9.7	8.0
13.	Beecham	Amoxil (250mg/5ml)	0.0	0.0	0.0	0.0	0.0	0.0
14.	Warner Lambert (Parke Davis)	Dilantin (100mg)	9.9	10.0	10.0	10.4	15.1	8.9
15.	Eli Lilly	Keflex (250mg)	10.0	23.2	6.0	9.0	8.9	15.5
16.	Abbott Laboratories	E.E.S. (400mg)	10.0	12.1	10.0	0.0	12.7	0.0
17.	Pfizer, Inc.	Feldene (20mg)	NFDA	AFDA	0.0	0.0	19.8	0.0
18.	Ciba-Geigy	Lopressor (50mg)	19.3	11.9	10.1	23.1	10.0	19.8
19.	Beecham	Amoxil (250mg)	0.0	0.0	0.0	0.0	0.0	0.0
20.	Upjohn	Xanax (0.5mg)	0.0	10.1	18.3	21.0	10.0	4.5

Source: Medi-Span

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* Prices cited are for quantities of 100 per package -- generally the most widely purchased size.

NFDA -- Not yet approved for sale by FDA
AFDA -- First approved for sale by FDA.

TABLE 7

PERCENTAGE PRICE INCREASES FOR BEST-SELLING PRODUCTS OF COMPANIES INVITED TO TESTIFY BEFORE THE SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT

	Price Increases	
Company/Products	1985	1986
1. Abbott Laboratories -- DP*		
Depakene	9.0	19.7
E.E.S.	(1.3)	1.9
Enduran	7.6	13.6
K-Lor	6.0	8.9
K-Tab	9.7	11.5
Tranxene	20.5	22.8
2. American Home Products -- DP		
Inderal	20.2	16.0
Premarin	15.0	23.3
Isordil-AWP**	8.0	14.6
Synalgos-AWP	21.0	21.0
LoOvral	9.1	10.2
Ativan	27.9	20.4
Ovral	12.2	11.4
Serax	27.9	27.4
3. Burroughs Wellcome -- AWP		
Actifed	14.5	9.3
Cortisporin	11.1	10.0
Empirin w/Codeine	9.0	6.5
Lanoxin	40.6	39.5
Neosporin	17.5	11.4
Septra	8.6	11.7
Zovirax-Oral	0.0	1.4
Zyloprim	18.2	0.0
4. Ciba -- DP		
Apresoline	15.0	29.2
Ludiomil	12.2	12.8
Ritalin	10.8	9.9
Ser-Ap-Es	7.4	30.2
Slow-K	8.0	5.0
Transderm Nitro	3.7	2.3
Geigy -- AWP		
Brethine	8.1	6.2
Lopressor	9.5	24.0
Tegretol	10.1	8.1

TABLE 7 (con't)

5. Glaxo, Inc. -- AWP		
Zantac	12.4	10.8
Ventolin	10.0	8.9
6. Eli Lilly and Co. -- AWP		
Darvocet-N	19.2	9.6
Ceclor	9.8	12.4
Darvon	19.2	9.6
Insulin I	6.1	7.1
Humulin	0.0	0.0
Keflex	9.8	13.9
Nalfon	9.8	12.0
7. Hoffmann-La Roche -- AWP		
Bactrim	9.2	12.6
Dalmane	15.0	12.8
Librax	21.1	12.8
Valium	17.0	12.8
Accutane	10.0	11.0
8. SmithKline Beckman -- AWP		
Dyazide	13.8	13.7
Tagamet	12.6	15.3
9. Sterling Drug -- AWP		
Danocrine	11.4	15.9
Neggram	17.7	20.3
Neo-Synephrine	18.2	23.4
Plaquenil	19.4	24.1
Talwin	18.3	18.7
Demerol	18.8	20.3
10. Warner-Lambert -- DP		
Dilantin	12.6	11.8
Meclomen	10.0	16.7
Procan SR	7.2	6.1
Benadryl	7.4	9.1
Centrax	15.0	15.0
Loestrin/Norlestrin	14.2	13.7
Anusol	9.9	8.2
Lopid	10.2	9.1
ERYC	9.2	0.8

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* DP = Direct Price
** AWP = Average wholesale Price

Source: Eberstadt Fleming Inc.

TABLE 8

TOP TWENTY-FIVE SELLING DRUGS IN THE U.S. IN 1986 (RETAIL AND HOSPITAL SALES)*

Drug	Sales (millions of dollars)	Company
1. Tagamet	553	SmithKline Beckman
2. Zantac	448	Glaxo
3. Naprosyn	287	Syntex
4. Dyazide	282	SmithKline Beckman
5. Keflex	279	Eli Lilly
6. Tenormin	254	ICI (Stuart)
7. Mefoxin	225	Merck
8. Procardia	223	Pfizer
9. Feldene	215	Pfizer
10. Xanax	214	Upjohn
11. Cardizem	210	Marion Labs.
12. Valium	208	Hoffmann-La Roche
13. Tylenol	205	Johnson and Johnson
14. Capoten	194	Squibb
15. Ceclor	194	Eli Lilly
16. Inderal	181	American Home Products
17. Lopressor	178	Ciba-Geigy
18. Clinoril	156	Merck
19. Transderm-Nitro	142	Ciba-Geigy
20. Aldomet	133	Merck
21. Premarin	124	American Home Products
22. Vancocin	116	Eli Lilly
23. Ativan	115	American Home Products
24. Motrin	115	Upjohn
25. Darvocet-N	114	Eli Lilly

* For purposes of this chart, all dosage forms and package sizes of the drug are combined to produce a total sales figure.

Source: International Marketing Services America, Limited

TABLE 9

PROFITS PER DOLLAR OF SALES (CENTS) AFTER TAXES

Year	All Manufacturing Corporations	Pharmaceutical Corporations*
1967	5.0	10.1
1968	5.1	9.7
1969	4.8	9.6
1970	4.0	9.4
1971	4.2	9.5
1972	4.3	10.1
1973	4.7	10.2
1974	5.5	12.2
1975	4.6	11.9
1976	5.4	12.2
1977	5.3	12.1
1978	5.4	12.5
1979	5.7	13.3
1980	4.9	13.2
1981	4.8	11.0
1982	3.5	13.1
1983	4.0	13.4
1984	4.6	13.2
1985	3.8	9.8
1986	3.7	14.5

* Note: For the purpose of this table, pharmaceutical corporations are defined as corporations primarily engaged in manufacturing biologicals, inorganic and organic medicinal chemicals, pharmaceutical preparations, and grading, grinding, and milling of botanicals.

Source: Quarterly Financial Reports for Manufactuirng, Mining and Trade Corporations, Federal Trade Commission (through 1981); U.S. Department of Commerce, Bureau of the Census (since 1982).

TABLE 9A

ANNUAL RATES OF PROFIT ON STOCKHOLDER'S EQUITY (PERCENT)
AFTER TAXES

Year	All Manufacturing Corporations	Pharmaceutical Corporations*
1967	11.7	18.7
1968	12.1	18.3
1969	11.5	18.4
1970	9.3	17.6
1971	9.7	17.8
1972	10.6	18.6
1973	12.8	18.9
1974	14.9	18.7
1975	11.6	17.7
1976	13.9	18.0
1977	14.2	18.2
1978	15.0	18.8
1979	16.4	19.3
1980	14.0	19.9
1981	13.7	16.8
1982	9.3	19.7
1983	10.6	20.3
1984	12.4	20.2
1985	10.2	15.2
1986	9.6	22.9

* Note: For the purpose of this table, pharmaceutical corporations are defined as corporations primarily engaged in manufacturing biologicals, inorganic and organic medicinal chemicals, pharmaceutical preparations, and grading, grinding, and milling of botanicals.

Source: Quarterly Financial Reports for Manufacturing, Mining and Trade Corporations, Federal Trade Commission (through 1981); U.S. Department of Commerce, Bureau of the Census (since 1982).

TABLE 10

PRICES FOR SELECTED TOP-SELLING PRESCRIPTION DRUGS: BRAND NAMES VERSUS GENERICS
(wholesale -- packages of 100)

Drug	1984	1985	1986
Aldomet 250mg tab	17.95	19.11	21.03
METHYLDOPA 250mg			
Company A	9.23	9.88	6.70
Company B	12.45	13.40	13.40
Aldoril -25 tab	24.43	26.63	29.83
METHYLDOPA/HCTZ 25mg			
Company A	NA	13.75	12.95
Company B	NA	NA	18.95
Ativan 1mg tab	24.23	31.20	40.99
LORAZEPAM 1mg tab			
Company A	NA	13.90	7.75
Company B	NA	15.70	15.70
Catapres 0.1mg tab	18.03	19.83	21.61
CLONIDINE HCL 0.1mg tab			
Company A	NA	NA	3.80
Company B	NA	NA	4.90
Dalmane 30mg	21.68	23.64	28.21
FLURAZEPAM 30mg			
Company A	NA	15.77	12.85
Company B	NA	NA	17.50
Darvocet N - 100	24.88	27.12	29.83
PROPOXYPHENE-N-100/APAP			
Company A	NA	12.00	10.50
Company B	NA	17.95	17.95
Diabinese 250mg	34.59	34.59	34.59
CHLORPROPAMIDE 250mg			
Company A	2.85	2.85	2.85
Company B	18.25	4.10	4.10

TABLE 10 (con't)

Inderal 40mg	17.04	19.51	23.60
PROPRANOLOL 40mg			
Company A	NA	10.16	4.42
Company B	NA	11.95	11.95
Indocin 25mg	29.33	31.76	35.38
INDOMETHACIN 25mg			
Company A	10.90	9.45	4.95
Company B	17.60	14.45	8.50
Valium 5mg	22.36	26.50	29.24
DIAZEPAM 5mg			
Company A	NA	13.75	12.95
Company B	NA	NA	18.95

GENERIC EQUIVALENTS INDICATED IN CAPITAL LETTERS

NA = drug not available in generic form through that generic manufacturer

Source: Brand name prices provided by Medi-Span
Generic prices provided by Generic Pharmaceutical Industry Association

NB: All brand and generic pharmaceutical companies requested that all manufacturer price information that they supplied be treated confidentially by the Subcommittee. In accordance with these requests, brand drug price data is from other sources, such as Medi-Span, and generic price information is not identified by company.

TABLE 11

PRICE CHANGES FOR SELECTED TOP-SELLING PRESCRIPTION DRUGS: BRAND NAMES VERSUS GENERICS

Brand Name	Date	Price change (%)	Generic Equivalent	Date	Price change (%)
Aldomet 250mg tab	1-1-85		Methyldopa 250mg	4/85-2/87	-27
	1-1-86	+10			
	1-1-87	+11			
Aldoril -25 tab	1-1-85		Methyldopa/HCTZ 25mg	2/86-2/87	-19
	1-1-86	+11			
	1-1-87	+11			
Ativan 1mg tab	1-11-85		Lorazepam 1mg	12/85-12/86	-52
	6-14-85	+11			
	11-13-86	+13			
Catapres tab 0.1mg	1-28-85		Clonidine HCL 0.1mg	5/86-2/87	-82
	2-3-86	+8			
	2-9-87	+9			
Dalmane 30mg	3-4-85		Flurazepam 30mg	12/85-11/86	-28
	1-6-86	+9			
	10-22-86	+8			
Darvocet-N-100	6-3-85		Propoxyphene-N-100/APAP	8/5-11/86	-19
	6-19-86	+9			
Diabinese 250mg	5-1-84		Chlorpropamide 250mg	10/84-12/86	-55
	6-1-86	+5			

TABLE 11 (con't)

Inderal 40mg	1-2-85		Propranolol 40mg	7/85-1/87	-78
	1-2-86	+6			
	10-1-86	+7			
Indocin 25mg	1-1-84		Indomethacin 25mg	4/84-11/86	-60
	1-1-85	+8			
	1-1-86	+11			
	1-1-87	+11			
Valium 5mg	3-4-85		Diazepam 5mg	8/85-2/87	-83
	1-6-86	+8			
	10-20-86	+8			

Source: REVCO D.S., INC.

These price changes were recorded for drugs purchased from pharmaceutical manufacturers by REVCO during the periods listed.

TABLE 12

PRICES CHARGED TO CONSUMERS WHO ARE AARP MEMBERS FOR LEADING BRAND NAME DRUGS AND GENERIC EQUIVALENTS

All prices are for a quantity of 100
Prices effective April 17, 1987

Aldomet 250 mg. Tab.	20.95
METHYLDOPA 250 mg.	9.95
Aldomet 500 mg. Tab	36.95
METHYLDOPA 500 mg.	18.95
Diabinese 250 mg. Tab.	29.70
CHLORPROPAMIDE 250 mg.	8.50
Inderal 10 mg. Tab.	11.35
PROPRANOLOL 10 mg.	5.50
Inderal 20 mg. Tab.	15.40
PROPRANOLOL 20 mg.	7.95
Inderal 40 mg. Tab.	19.75
PROPRANOLOL 40 mg.	9.95
Inderal 80 mg. Tab.	32.20
PROPRANOLOL 80 mg.	17.95
Indocin 25 mg. Cap.	31.95
INDOMETHACIN 25 mg.	13.95
Lasix 40 mg. Tab.	11.95
FUROSEMIDE 40 mg.	5.95
Motrin 400 mg. Tab.	12.95
IBUPROFEN 400 mg.	7.95
Norpace 100 mg. Cap.	26.10
DISOPYRAMIDE	18.95
Valium 5 mg. Tab.	26.95
DIAZEPAM 5 mg.	9.50

GENERIC EQUIVALENTS INDICATED IN CAPITAL LETTERS

Source: American Association of Retired Persons Pharmacy Service

27

U.S. House of Representatives
Committee on Energy and Commerce
Room 2125, Rayburn House Office Building
Washington, DC 20515

February 20, 1987

Dear ,

As you may know, the Subcommittee on Health and the Environment is concerned about the rise in the prices charged for prescription drugs in the United States during the past six years. We explored various aspects of this issue at a hearing on July 15, 1985 and indicated that we planned to revisit the issue at a later point. We have decided to hold another hearing this year. It is tentatively scheduled for April 6, 1987.

In order to explore the explanations given for these price increases by several pharmaceutical company witnesses at our July 15 hearing, we have decided that it is necessary to ask 25 of the major pharmaceutical manufacturers to respond to a questionnaire regarding their pricing policies. The information derived from the questionnaire will be aggregated by the Subcommittee in order to publish a report that provides an industry-wide picture of prescription price increases and the rationale that has been given for them. *The Subcommittee will not release any data from the questionnaire with respect to individual responses and will consider all data relating to individual companies to be confidential*.

The Subcommittee requests that you answer all questions. We would appreciate your response no later than March 13, 1987. We appreciate your cooperation. If you have any questions, please feel free to contact either Bill Corr or Bob Adler at (202) 226-7620.

With every good wish, I am,

Sincerely,

Henry A. Waxman

HENRY A. WAXMAN
Chairman, Subcommittee on
Health and the Environment

HAW/ban

QUESTIONNAIRE REGARDING PRESCRIPTION DRUG PRICES

1. What were your company's total revenues in the United States from the sale of prescription drugs for each year 1981-1986?

2. What percent of the revenues referred to in question 1 for each year 1981-1986 were derived from higher prices, as opposed to increased unit sales or the introduction of new products?

3. What were your company's total expenditures in the United States for research and development for prescription drugs for each year 1981-1986? Of the amount for each year, what did your company spend on new chemical entities, i.e., active ingredients never before approved by FDA (count only the expenditures for the first approval of the new chemical entity)?

[For purposes of this question, the term "research and development" *excludes* marketing and detailing expenditures and *includes* basic and applied research as well as development activities carried on or supported in the pharmaceutical, biological, chemical, medical and related sciences, including psychology and psychiatry, if the purpose of such activities is concerned ultimately with the utilization of scientific principles in understanding diseases or in improving health. This definition is the same as that used by the Pharmaceutical Manufacturers Association in its *Annual Survey Report of the U.S. Pharmaceutical Industry*.]

4. What is the dollar amount of the tax credit taken by your company for "research and experimental expenditures" for prescription drugs for each year 1982-1986?

5. What were your company's total expenditures in the United States for marketing and detailing for prescription drugs for each year 1981-1986? For purposes of this question, the term "marketing and detailing" excludes research and development and includes all activities relating to advertising, sales, promotion, exhibitions, conventions, market research and detail work.

6. For each year during the period 1981-1986 and for each of your company's ten top-selling prescription drugs (by dose and package size), state the amount and percent by which your company increased the price of the drug over the previous year (for example, for 1981, state the percentage increase by which your company increased the price of the drug over the year 1980).

7. Provide the price in the United States as of January 1, 1987 of your company's ten top-selling prescription drugs (i.e., those producing the greatest sales revenue) by dose and package size. (For purposes of this question, please treat different dosage and package sizes of a drug as separate drugs.) For each of these drugs and for the same date, provide in dollars the prices of each drug in each of the five foreign countries in which you have the greatest sales revenue for each drug.

8. Does your company own or control any company that makes generic drugs? Provide the name of the company that makes generic drugs. Does your company own or control a subsidiary that owns or controls a company that makes generic drugs? Provide the name of the subsidiary and the company that it owns or controls that makes generic drugs.

Mr. **Waxman**. This report is available today. It indicates the findings of the staff through a survey of drug companies that have been asked to give us information about their price increases and their R&D costs.

Mr. **Whittaker**. Mr. Chairman, can I inquire on the part of the minority if we had access to that report and had an opportunity to review it?

Mr. **Waxman**. I would hope it had been shared by the minority staff but this was prepared by the staff of the subcommittee for the Chairman. It is a survey we have taken of the various pharmaceutical companies.

Mr. **Whittaker**. I would like the record to show that the minority in fact has not had an opportunity to look at that report.

Mr. **Waxman**. The record will so note.

The first witnesses I'd like to call forward to testify are Mr. Jack Guildroy, American Association of Retired Persons, accompanied by Judith Brown, Policy Specialist for the AARP and Mr. William Hutton, Executive Director of the National Council of Senior Citizens, who will be accompanied by Benjamin Gordon, Staff Economist.

If you would please come forward and take seats at the table. We want to welcome you to our subcommittee hearing this morning. Your prepared statements will be made part of the record in full. What we would like to ask each of you to do is to summarize that testimony in no more than 5 minutes so that we will have a full opportunity for questions and answers and to hear all the other witnesses.

Mr. Guildroy, why don't we start with you.

STATEMENTS OF JACK GUILDROY, MEMBER, NATIONAL LEGISLATIVE COUNCIL, AMERICAN ASSOCIATION OF RETIRED PERSONS, ACCOMPANIED BY JUDITH BROWN, POLICY SPECIALIST; AND WILLIAM R. HUTTON, EXECUTIVE DIRECTOR, NATIONAL COUNCIL OF SENIOR CITIZENS, ACCOMPANIED BY BENJAMIN GORDON, STAFF ECONOMIST

Mr. **Guildroy**. Thank you, Mr. Chairman. My name is Jack Guildroy. I'm a member of the National Legislative Council of the American Association of Retired Persons. With me is Judith Brown who deals with pharmaceutical issues for AARP.

AARP is very appreciative of the Committee's invitation to be here today. We are a membership organization representing over 25 million Americans age 50 and older. AARP has always maintained a keen interest in pharmaceutical issues, since older persons consume a disproportionately high amount of prescription drugs.

We commend you, Chairman Waxman and other members of the Committee, for focusing attention today on continued price increases by the pharmaceutical industry, and uncompetitive prices of some large drug manufacturers, who disparage the use of generic equivalence to their brand name products.

As this Committee's July 1985 hearings on these same issues made clear, prices for prescription drugs began to sky rocket in 1981 and have far out paced other items in the Consumer Price Index ever since. It was AARP's hope that congressional scrutiny and media attention might serve to moderate the upward trend in prescription drug prices but that trend has continued unabated.

Drug companies set high prices for new drugs coming on the market and increase their prices sharply and frequently because they discovered they can. The United States is virtually the last country in the world without some form of control over prescription drug prices. Consumers who are more often elderly are held hostage by whatever pricing structure a pharmaceutical company wishes to adopt.

Price increases in recent years seem to ignore the fact that prescription drugs are necessary, not discretionary items.

Patients can't put off buying essential drugs until there is a sale at their pharmacy or until they have enough money saved. AARP has long urged that compassion be shown in drug pricing, since the profits and activities of the multi-billion dollar drug industry are supported almost entirely by sick, often elderly people.

In 1985, expenditures for prescription drugs were the second highest out of pocket costs for older Americans, led only by the cost of long term care. In 1986, drug expenditures for the population aged 65 and over were projected to be $9 billion. Of that, $7.3 billion, 81 percent, was estimated as out of pocket expenses for the elderly.

We have included detailed figures on the increase in out-of-pocket spending for older Americans in an attachment to our formal statement. We listed many of the individual price increases that have contributed to the overall burden of high drug costs and some of the rates and frequencies of the increases are alarming.

For example, Inderal, from 1983 to 1986, 7 increases amounting to a rise of 118 percent. Lanoxin, from 1983 to 1986, 5 increases, totaling an increase of 168 percent. Lopressor, from 1983 to 1986, 6 increases, a rise of 79 percent.

AARP shared the hope of Congress in 1984 that more competition would be seen in the pharmaceutical marketplace by removing obstruction for generic approval but our worse fears were quickly realized. We saw millions of dollars poured into activities to maintain brand loyalty and to unfairly disparage generic competition.

We have been very vocal and visible in responding to this anti-generic campaign waged by some brand name manufacturers. Efforts to persuade health professionals that generics are unsafe and/or ineffective have spawned a new realm of, dare we use the term, "innovation," in the drug industry. The deceptive tactics we have seen since the passage of the 1984 legislation are too exhaustive to list in full even in our formal statement.

We continue to fight anti-generic messages on many fronts. From a nationally syndicated TV show, Hour Magazine, this January, that promised viewers throughout the day that they would learn of the "dangers of generic drugs," to the director of a State pharmaceutical association telling AARP leaders this February that generic drug companies can "mix active ingredients with cement."

AARP believes the time has arrived for policy makers to seriously consider alternatives to our present system of financing prescription drug costs, especially for the elderly and alternatives to the current pricing structure which amounts to what the market will bear for these essential, often live-saving products.

We believe that a restructuring of our current system deserves serious consideration. AARP has been closely studying the Canadian system and believes that the savings demonstrated under the compulsory licensing law offers the United States an appropriate market-oriented model for moderating the trend in escalating prescription drug prices.

Policy makers in the U.S. must begin to help make access to prescription drug therapies a priority for the Nation's health care system.

Thank you, Mr. Chairman.

[Testimony resumes on p. 234.]

[The prepared statement of Mr. Guildroy follows:]

Testimony
# of the
American Association of Retired Persons

The American Association of Retired Persons (AARP) appreciates the Committee's invitation to be here today. AARP is a membership organization representing 25 million Americans age 50 and older. AARP has always maintained a keen interest in pharmaceutical issues since older persons consume a disproportionately high amount of prescription drugs. Although those age 65 and older constitute 12% of the population, they consume 30% of the nation's prescription drugs. AARP's interest in the drug arena is on access to safe, effective and affordable drugs.

We commend you, Chairman Waxman, and other members of the Committee for focusing attention today on continued price increases by the pharmaceutical industry and uncompetitive practices of some large drug manufacturers to disparage the use of generic equivalents to their brand name products.

Our testimony today will discuss:

- o Pharmaceutical industry pricing practices;
- o Prescription drug expenditures for older persons;
- o Recent prescription price increases;
- o Anti-generic drug activities; and,
- o Alternatives to our present system.

Industry Pricing Practices

As this Committee's July 1985 hearings on these same issues made clear, prices for prescription drugs began to skyrocket in 1981 and have far outpaced other items in the Consumer Price Index (CPI) ever since. Between the period of January 1981 to June 1985, prices for prescription drugs rose 56%, compared to the rise in the overall CPI of 23%. It was AARP's hope that Congressional scrutiny and media attention might serve to moderate the upward trend in prescription drug prices, but that trend has continued unabated.

In 1986, prescription prices were again the highest of all medical care components, increasing at a rate of 8.6% last year, compared to the overall rise in the CPI of 1.9%. [1]

Drug companies set high prices for new drugs coming on the market and increase their prices sharply and frequently because they discovered they can. The United States is virtually the last country in the world without some form of control over prescription drug prices. Prescription drug consumers, who are more often elderly, are held hostage by whatever pricing structure a pharmaceutical company wishes to adopt. Price increases in recent years seem to ignore the fact that prescription drugs are necessary, not discretionary items.

Patients cannot put off buying essential drugs until there is a sale at their pharmacy or until they have more money saved. AARP has long urged that compassion be shown in drug pricing, since the profits and activities of the multi-billion dollar drug industry are supported almost entirely by sick, often elderly people.

There are few, if any, free market forces operating in the prescription drug industry. The decisions as to which product will be prescribed and, in most states, if a generic equivalent drug may be substituted rests with the doctor. Although the term "consumer" is frequently used to describe those who take prescription drugs, the consumer in the pharmaceutical marketplace has little decision-making power. They just get to pay the bills. The bills, especially for older Americans, are steep. In 1985, the nation's total expenditures for prescription drugs and medical sundries were $28.5 billion. Of that sum, $21.7 billion (77%) was paid directly by consumers. [2] In 1985, expenditures for prescription drugs were the second highest out-of-pocket cost for older Americans, led only by the cost of long term care.

Expenditures by Older Americans

Data about prescription drug costs for specific populations is difficult to obtain. A study commissioned by AARP projected 1986 drug expenditures for the population age 65 and over to be $9 billion. Of that, $7.3 billion (81%) was estimated as out-of-pocket expenses for the elderly. [3]

Two AARP national surveys conducted in 1985 [4] and 1986 [5] sought to assess the impact of increasing drug prices on older Americans. Of those aged 65 and older who were taking any prescription drugs regularly, over half (55%) said they received no assistance in paying for those drugs from insurance or other health coverage. In just one year for this group, there appeared a 42% increase in the percentage of persons who paid the most money out-of-pocket (over $480 per year). We have included more detailed figures on out-of-pocket spending as an attachment to this testimony.

In both 1985 and 1986, even of those older persons who received assistance in paying their prescription drug bills, 71% still had to pay some money out-of-pocket.

The cost of drugs also emerged as a major factor in patients' decisions not to fill a prescription ordered by their doctor. In 1982, AARP asked survey respondents who had declined to get a prescription filled for their reasons: cost was the fourth reason given. [6] When asked again in 1986, cost was given as the second most important reason. Clearly, cost has gained in prominence as a reason for non-compliance with prescribed drug regimens.

Recent Price Increases

Some of the price increases that have contributed to the overall burden of high drug costs are listed by individual drug products as an attachment. The manufacturers' price increases were compiled by the AARP Pharmacy Service for some of their top selling drugs. Some of the rates and frequencies of the increases are alarming:

Product (Manufacturer)	Number of Price Increases	Total % Increase
Inderal 40 mg (Ayerst)	7 increases from 1/83 - 10/86	118%
Lanoxin .125 mg (Burroughs-Wellcome)	5 increases from 9/83 - 3/86	168%
Lopressor 50 mg (Geigy)	6 increases from 3/83 - 7/86	79%
Dyazide (cap) (SKF)	5 increases from 6/83 - 3/86	70%
Tenormin 50 mg (Stuart)	7 increases from 6/82 - 9/86	57%

We have seen no moderation in price increases when the patent for a brand product expires and the product is subject to generic competition. Contrary to accepted market theory, brand name prices continue going up when met with competition. In a rush to offset decreased market share, many companies raise prices significantly in the time period before the brand product goes off patent. In this way, consumers get burned twice: they must pay whatever price demanded while the manufacturer has a monopoly, then they must pay an artificially inflated price for the coming generic product, since generics are usually priced as a percentage of the brand name.

Anti-Generic Campaign

AARP shared the hope of Congress in 1984, with the passage of the Drug Price Competition and Patent Term Restoration Act, that more competition would be seen in the pharmaceutical marketplace by removing obstructions for generic approvals. We hoped that enactment of the legislation would exert downward pressure on prescription drug prices. Our worst fears were realized quickly, however, when we saw millions of dollars being poured into activities to maintain brand loyalty and unfairly disparage generic competition.

AARP has been very vocal and visible in responding to this "anti-generic" campaign waged by some brand name manufactures. Efforts to persuade health professionals that generics are unsafe and/or ineffective have spawned a new realm of "innovation" in the drug industry. The deceptive tactics we have seen since the passage of the 1984 legislation are too exhaustive to list in full. The following list, however, should provide an indication of the scope of anti-generic activities:

- Blatent misrepresentations made by PMA member companies to state legislative committees. This is of special significance to AARP when false statements are made in the context of discussions surrounding states' adoption of programs to assist marginally poor elderly in paying their prescription drug bills, as was the case in New York.

- False and misleading advertising in professional journals which inferred that generics are, in various unsubstantiated ways, inferior to brands.

- Covert funding of supposedly "independent" practitioners and academicians to go on the speaking circuit to cast false aspersions on the safety and quality of generic drugs.

- A series of unsubstantiated anti-generic articles in a tabloid, Medical Tribune, that is sent free to 150,000 doctors. The publication is supported entirely by brand name industry funds and, indeed, its publisher owns one of the major advertising firms that represents brand name companies.

The FDA was successful in stopping some of the anti-generic activities, such as misleading advertising and misrepresentations made to some state formulary committees. We commend the FDA, and in particular, the Division of Drug Standards under the leadership of Dr. Peter Rheinstein, for vigilance in their attempts to counter the anti-generic campaign. This office also produced a valuable document, "Myths vs. Facts About Generic Drugs," which was intended to inform health professionals that they were the objects of a misinformation campaign and to set the record straight. Unfortunately, FDA was unsuccessful in placing the article in any journal for health professionals since editors were reluctant to anger a major source of revenue; brand-name advertisers. It was for this reason that AARP paid for placement of FDA's "Myths vs. Facts" article in the New England Journal of Medicine last October. So far, hundreds of doctors have written in to AARP to request thousands of reprints of the article. It is apparent to us that doctors welcome such information from an unbiased, authorative source such as the FDA. We have included the article as an attachment to this testimony.

We had hoped that the conference on bioequivalence held by the FDA last fall and widely attended by all facets of the pharmaceutical area would put the anti-generic campaign to rest. It was an opportunity for anyone to come forward with any scientific data to show that there were problems in the FDA approval process for generics or that there were problems in actual clinical practice using generic drugs. Not one shred of evidence emerged to show that any problems exist with the generic drugs that FDA has approved as bioequivalent to their brand name counterparts.

Despite the FDA bioequivalence conference, we are still fighting anti-generic messages on many fronts. From a nationally syndicated TV show, Hour Magazine, this January that promised viewers throughout the day that they would learn of the " dangers of generic drugs," to the director of a state pharmaceutical association telling AARP leaders this February that generic drug companies can "mix active ingredients with cement."

These methods have been predictably successful in influencing public opinion about generic drugs. In AARP's 1985 and 1986 national surveys, we asked if respondents believed the government has the same standards for safety, effectiveness and quality for both generic and name brand drugs. In just one year, about 10% of respondents shifted from agreeing that government standards are the same into the "Don't Know" category. This translates into a 50% increase in the percentage of persons who are now confused and, indeed, "don't know."

Alternatives to Our Present System

AARP believes that the time has arrived for policymakers to seriously consider alternatives to our present system of financing prescription drug costs, especially for the elderly, and alternatives to the current pricing structure which amounts to "what the market will bear" for these essential, often life-saving, products.

The current discussions involving catastrophic health insurance coverage provide a framework for expansion of Medicare to include a prescription drug benefit. Such a benefit would add significantly to the value of a "catastrophic" package by addressing directly one of the major sources of high out-of-pocket costs for the Medicare population. A Medicare prescription drug benefit should be phased in and should be built around a sound administration structure and incorporate cost containment mechanisms.

A government system of cost containment for pharmaceuticals was in place as the MAC (Maximum Allowable Cost) program. As you know, this program which set limits on the amount the government would reimburse for prescription drugs under Medicaid, is essentially dead. Several proposals are being considered to replace or revitalize the MAC program although deliberations have been slow regarding which of the proposals are the most feasible. AARP hopes that legislative interest will serve to speed up and influence the deliberations so that the most effective cost containment system is put into place quickly.

Clearly, generic utilization and overall cost containment measures are essential to any federal or state government program seeking to provide prescription drug benefits.

In the general pharmaceutical marketplace, however, AARP believes that a restructuring of our current system deserves serious consideration. We are pleased that the Committee has invited Dr. Harry Eastman from Canada to discuss the Canadian system of compulsory licensing for pharmaceuticals. The compulsory licensing system, enacted in 1969, introduced price competition into the Canadian pharmaceutical industry. At that time, Canada was experiencing among the highest prices in the world. Now, the U.S. rather stands alone. The lower prices acheived by competition enabled Canada's Provinces to extend free prescription drug benefits to social welfare recipients and senior citizens.

AARP has been closely studying the Canadian system and believes that the savings demonstrated under the compulsory licensing law offers the United States an appropriate market-oriented model for moderating the trend in escalating prescription drug prices. Policymakers in the U.S. must begin to help make access to prescription drug therapies a priority for the nations's health care system.

REFERENCES

[1] Bureau of Labor Statistics, U.S. Department of Labor. Figures cited compare average annual increases for 1985 and 1986 for all urban consumers.

[2] Health Care Financing Administration, U.S. Department of Health and Human Services.

[3] AARP Research Project: "The Role of Medicare in Financing the Health Care of Older Americans," conducted by ICF, Incorporated, Washington, D.C. July 1985.

[4] AARP Seventh Annual Survey of Older Americans, conducted by Hamilton & Staff, Washington, D.C. November 1985. National telephone survey of 1,500 persons age 45 and older.

[5] AARP Eighth Annual Survey of Older Americans, conducted by Hamilton & Staff, Washington, D.C. December 1986. National telephone survey of 2,000 persons age 45 and older.

[6] AARP National Survey, "Prescription Drugs: A Survey of Use, Attitudes and Behavior," conducted by Applied Research Techniques, Parsippany, NJ. November 1982. National telephone survey of 1,001 persons age 45 and older.

Attachment I

MONTHLY OUT OF POCKET EXPENDITURES FOR PRESCRIPTION DRUGS FOR PERSONS 65+ WHO TAKE AT LEAST ONE DRUG REGULARLY

Data from Two National Surveys Commissioned by the American Association of Retired Persons

FIGURE 1

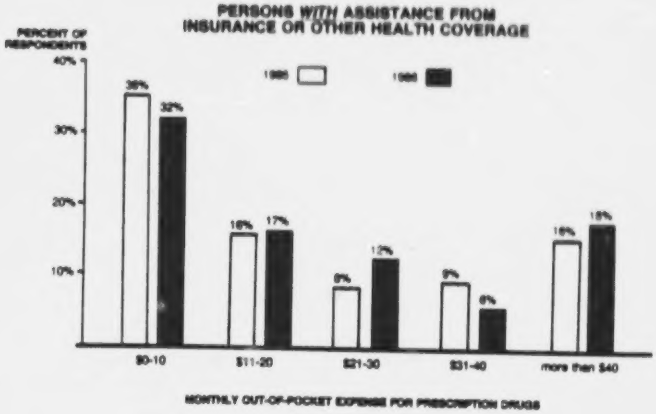
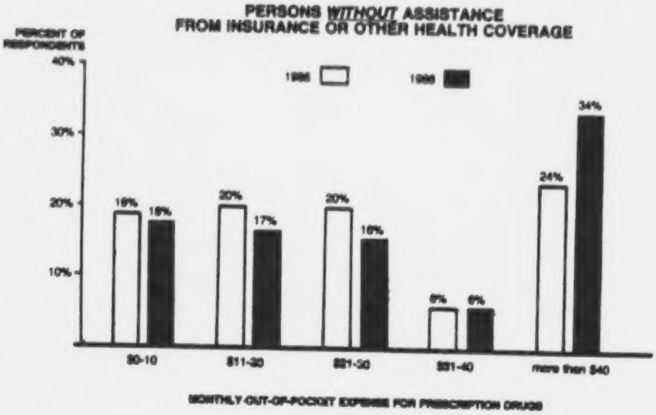

PERSONS *WITH* ASSISTANCE FROM INSURANCE OR OTHER HEALTH COVERAGE

FIGURE 2


PERSONS *WITHOUT* ASSISTANCE FROM INSURANCE OR OTHER HEALTH COVERAGE

AARP
PHARMACY
SERVICE

Retired Persons Services, Inc.

Prince Street
Alexandria, Virginia 22314
(703) 684-0244

JOHN R. McHUGH
President

September 30, 1986

The following list displays percentage price increases of our top selling drugs based on comparing the largest sizes available at the time of the price increase. (Manufacturer price increases).

ALDOMET 250mg. **(MSD)**	5/82	12%
	1/83	9.8%
	1/84	9.8%
	1/85	6.5%
	1/86	10%
	Cumulative increase	58.2%
DIABINESE 250mg. **(Pfizer)**	9/82	9.7%
	8/83	6.3%
	5/84	10%
	1/85	10%
	6/86	5%
	Cumulative increase	48.2%
DIPYRIDAMOLE 25mg. **(Generic)**	NONE*	
DIPYRIDAMOLE 50mg. **(Generic)**	NONE*	
DYAZIDE **(SKF)**	6/83	12%
	1/84	12.1%
	10/84	10%
	7/85	12%
	3/86	10%
	Cumulative increase	70.2%

FELDENE 20mg. (Pfizer)	8/83....................12% 10/84....................12% 6/85....................12% Cumulative increase...40.5%
FUROSEMIDE 40mg. (Generic)	NONE*
HYDROCHLOROTHIAZIDE (Generic)	NONE*
IBUPROFEN 400mg. (Boots)	1/84....................6.2% 5/84....................5.9% 7/84....................29.1% Cumulative increase...45.2%
INDERAL (Ayerst)	1/83....................9.9% to 12.5% 9/83....................15% 3/84....................11.9% 1/85....................14.5% 6/85....................10% 1/86....................12% 10/86....................8% Cumulative increase...117.6%
ISOSORBIDE 10mg. (Generic)	NONE*
LANOXIN 0.25mg. (BW)	9/83....................24.9% 2/84....................30% 10/84....................15% 4/85....................20% 3/86....................25% Cumulative increase...180.1%

LANOXIN 0.125mg.
(BW)

9/83...................24.9%
2/84...................29.7%
10/84..................15%
4/85...................20%
3/86...................20%
Cumulative increase...168.3%

LOPRESSOR 50mg.
(Geigy)

3/83...................9.9%
2/84...................10%
10/84..................12%
5/85...................10%
2/86...................10%
7/86...................9%
Cumulative increase...78.6%

LOPRESSOR 100mg.
(Geigy)

3/83...................9.9%
2/84...................10%
10/84..................12%
5/85...................10%
2/86...................8%
7/86...................4.5%
Cumulative increase...68.1%

NAPROSYN 375mg.
(Syntex)

2/83...................7%
10/83..................4%
2/84...................3.9%
11/84..................5%
7/85...................5%
6/86...................6%
Cumulative increase...35.1%

NORGESIC FORTE
(Riker)

9/83...................5%
3/84...................10%
9/84...................5.1%
3/85...................10%
9/85...................5%
3/86...................12%
9/86...................15%
Cumulative increase...80.6%

PROCARDIA 10mg.
(Pfizer)

1/83..................9%
2/84..................9.7%
1/85..................9.8%
6/86..................8%
Cumulative increase...41.8%

QUINIDINE 3gr.
(Generic)

NONE*

SLOW-K
(Ciba)

7/83..................9.1%
9/84..................5%
1/85..................5%
1/86..................5%
Cumulative increase...26.3%

TAGAMET 300mg.
(SKF)

3/82..................N/A
10/82..................9.8%
7/84..................17.3%
4/85..................10%
2/86..................10%
Cumulative increase...55.9%

TENORMIN 50mg.
(Stuart)

6/82..................12%
1/83..................4%
1/84..................9%
1/85..................9%
9/85..................5%
4/86..................4%
9/86..................4%
Cumulative increase...57.2%

*There have been no price increases of these generics for the past 2-3 years. In fact, there have been decreases in some.

STATEMENT OF WILLIAM R. HUTTON

Mr. Hutton. Thank you, Mr. Chairman. As you reported earlier, thank you for the privilege of putting our entire testimony into the record. I would like to deal for the next few minutes with some broader opinions.

I am Bill Hutton, executive director of the National Council of Senior Citizens, which is a federation of over 4,800 senior citizen clubs with over 4.5 million members. I have been testifying before committees of the Congress, both Houses, for many years, and mostly on the problems of the elderly and particularly about their concerns with regard to health.

Sitting next to me is Ben Gordon, our staff economist, who for many years was the staff economist of the Senate Small Business Committee. Actually he was on there for 25 years. He worked on problems of monopoly, government patent policy, government procurement, and was associated with the massive 10-year drug investigation conducted by that Committee's Monopoly Subcommittee.

We are submitting for the record a statement concerning the drug industry's research and development activities, the costs of which the industry advances as a justification for the unconscionable high prices of drugs.

The high cost of drugs has a particularly devastating effect on the elderly, who make up 11 percent of the population, but account for 30 percent of expenditures for prescription drugs. In addition, for 75 percent of the elderly, the cost of prescription drugs represents their largest out-of-pocket expenses. In many cases, a painful choice has to be made among medicine, food, rent, electricity and other necessities.

Since the use of medical care by the elderly is much greater than that of the non-elderly, the elderly are much more adversely affected by high drug costs than other elements in our population. The cost of drugs, vital to older Americans for treating such chronic conditions as heart disease, high blood pressure, and arthritis have risen more than twice the rate of inflation. Between January 1981 and June 1985, the Consumer Price Index rose 23 percent, while prescription drug prices rose by 56 percent.

The majority of our seniors pay $200 to $400 annually for prescription drugs, but some pay that much per month. The elderly with incomes of $12,000 to $15,000 pay 6 times as much out-of-pocket for prescription drugs than any other age group.

Medicaid provides coverage for outpatient prescription drugs for the very poor of our population. About 11 percent of our elderly are in this group, but many millions of the elderly have incomes above Medicaid eligibility levels and just above the poverty level. These are the people who are left financially strapped by drug costs.

We appreciate, Mr. Chairman, your sponsorship of legislation for an amendment for an expanded Medicaid prescription drug benefit; however, as important as this is, it will still not address the problems of the estimated 8 million older people considered to be economically vulnerable.

To address their problems, the only solution is to expand Medicare to cover outpatient prescription drugs. Drug coverage under

Medicare would be of great assistance not only to the elderly, the disabled, and the poor, but would also help in other important ways every person who uses prescription drugs.

As stated in our submission to the subcommittee, we believe that drug coverage under Medicare with the formulary list of medically necessary drugs and utilization review would be very helpful in reducing drug costs, improving prescribing patterns, and improving the quality of research and development for the following reasons:

(a) A formulary of drugs, which are considered by medical experts to be medically necessary and superior in the treatment of specific medical conditions, would serve as an educational device. Practicing physicians have no way of comparing the relative safety and efficacy of drugs. They are continually assaulted by drug company advertising and promotion. A formulary could be of great value to physicians in adding to their knowledge of the safety and efficacy of drugs.

(b) Drug companies, if they wish to get their drugs on the formulary, would channel their R&D into those kinds of drugs that have a reasonable chance of getting on the formulary. This would tend to reduce the cost of R&D allocated for the development of duplicative, unnecessary, and second-rate drugs.

(c) The cost of drugs to the elderly would decline, and costs under Medicare could be controlled through competitive bidding.

Drugs, if used properly, can be very cost-effective. The president of the PMA gave an example to this subcommittee of beta-blocking agents, the use of which—these better agents—I believe have helped society annually about $2.5 to $4.4 billion. An unpublished study by the School of Pharmacy of the University of South Carolina found that under a program of drug coverage for the elderly, Medicare payments to New Jersey residents were, on the average, $283 less than were payments to residents of 22 counties in Eastern Pennsylvania where no such program existed.

Mr. Chairman, this concludes our oral statement. We'd be very happy to respond to any questions you may have.

[Testimony resumes on p. 252.]

[The prepared statement of William Hutton follows:]

Testimony Before the

United States House of Representatives
Subcommittee on Health and the Environment

by

William R. Hutton, Executive Director
National Council of Senior Citizens
925 15th Street, N.W.
Washington, D.C. 20005

April 21, 1987

There is no end to the ingenuity of the drug companies in exploiting the American people. As we have shown when we appeared before this Subcommittee on July 15, 1985, with specific and concrete examples, the international drug companies are discriminating against the American people by charging higher prices for drugs in the United States than they charge for the same drug manufactured by the same firm, in the same plant, and sold under the same brand name in foreign countries.

When pressed to justify these differences in prices, the president of the Schering Company, a major drug firm, told the Monopoly Subcommittee of the Senate Small Business Committee: "But the living standards and purchasing power of people abroad differ greatly from those in our country."1/

In other words, they charge what the traffic will bear. These discriminatory practices have been going on for many years.

But this is not all.

Tax Imposed on Public to Finance R&D Programs

In addition to these outrageous practices, the drug companies are fleecing the public by continually and ruthlessly raising prices of widely-used drugs, particularly those used by the elderly. The increases are huge and unconscionable and cannot be justified on any economic basis. Included are drugs for chronic diseases, such as antihypertensives, anti-inflammatories, heart and ulcer drugs. We cannot understand why a drug like Rufen, an anti-inflammatory marketed in the U.S. by Boots (a British company) should increase its price by 45 percent in a six-month period--from January to July, 1984.

Why was the price of Inderal (propranolol) raised by 117.6 percent from January, 1983 to October, 1986? This drug was invented by the Imperial Chemical Industries of Great Britain and licensed to Ayerst Laboratories, a division of American Home Products.

What is Burroughs-Wellcome's justification for raising the price of Lanoxin 0.25 mg. (a heart drug) by 180.1 percent in less than a three-year period?

The drug companies claim that the cost of research has been going up. But the research for these and other drugs was done many years ago. The answer, acknowledged by the industry witnesses before your Subcommittee, is that the American people are paying twice for research and development: once for the research and development embodied in the products they buy, and a second time by paying for research and development for drugs which they may never use. In other words, the drug industry is levying a tax on the American public to pay for its research program in advance. This tax cannot be imposed in most industrialized countries because drug prices are controlled directly or indirectly. The United States and South Africa are the only industrialized countries in the world which have no mechanism to protect the public against high drug prices. Combined with the fact that the products of this industry are insensitive to price changes, the drug companies are in a position to force the American public to finance their research and development programs. In essence, the risks of failure are borne by the public, not the stockholders. In a private enterprise system, the justification of profits is risks; if there is no risk, there should be no profits. This industry enjoys very high profits without risk, a violation of the tenets of a private enterprise system. What we see here is the socialization of risk and the privatization of profits. This is an example of having your cake, eating it and seeing it grow——all at the same time.

Quantity of Research and Development (R&D)

Testimony by industry witnesses before this Subcommittee in July, 1985, estimated that, on the average, it cost 91, 94 and 100 million dollars to bring a drug to market. The industry does not tell us what those figures mean. Arthur D. Little, Inc., in a 1983 study,[2/] estimated that the cost of bringing a new molecular entity to market was about $11 million at a time when the industry was using a figure of $70 million. We suggest that the figures the industry uses are fictional, without any basis in fact and probably conceal much of what is really advertising.

According to testimony by two medical directors of two large drug firms, in the early '60s, before the Senate Judiciary Committee,[3] most of what the industry calls research is not research at all, but product development. In fact, one of the scientists recommended that the drug companies be required "to clearly identify expenditures for research as those which are devoted to basic studies," adding that "this should markedly decrease the justification for some of the very high prices."[4] He also deplored the waste of talent of well-trained and capable scientists employed by the drug companies. He claimed that the talents of many of these fine scientists are being used on patent bypassing, chemical manipulations and on inconsequential change to existing, established drugs.

We believe that the suggestion of the former medical director is even more relevant today. Since the drug companies are justifying their huge price increases by expenditures on what they claim as "R&D," and since they are taxing us to finance their research program in advance, then the public ought to know how the money is being spent. We, therefore, urge that complete and detailed information be secured from the industry on exactly what the money is being spent on.

SCRIP (issue of September 9, 1985, p. 19), the well-known British Pharmaceutical Journal, states that: "But the earnestness with which companies go about their R&D and the rigorousness of the discipline applied is in need of examination."

Poor Quality of Research

We do know that money is being wasted. According to the Food and Drug Administration (FDA) the vast majority of drugs coming on the market during the nine-year period 1974-1982 make very little or no contribution to improving medical practice and the health of the public. If we consider only the new molecular entities (NME), we find that only 26 of 185 drugs in this category (14.1 percent) offer important therapeutic gain over existing drugs.[5]

No improvement can be expected in the immediate future because, of the 922 new molecular entity drugs in the clinical testing process as of October 1982, only 23 (2.5 percent) are judged by FDA scientists to have the potential for important therapeutic gain.[6]

The records of the FDA, therefore, show the results of the "R&D" performed by the drug companies and it is not encouraging. Money and talent are being used to provide a superfluity of duplicative, unnecessary and inferior drugs.

The testimony before this Subcommittee of Mr. George De Mott, Vice President of American Home Products, is a good case in point. He stated that, "While the major portion of our initial research cost is in intangibles, the total investment is not without its tangible aspects. For example, in the last five years, we have built a $22 million research facility in Pennsylvania; a $45 million research and development center in New Jersey; and expanded, at a cost of $33 million, our research and development facilities in New York, to name only those in the United States.

"We now have over 2,400 scientists and technicians involved in research and development, compared to 1,500 only five years ago. In fact, our total research expenditures have increased by 116 percent in the same period.[7] Yet, despite the large expenditures for R&D claimed by American Home Products, FDA records show that the quality of the R&D is dismal. During the eleven-year period 1975-1985,* this company marketed only one new molecular entity which offered a significant therapeutic gain. This is generally the kind of research for which the pubic is involuntarily being forced to support through high prices. Incidentally, the widely used and important heart drug propranolol (Inderal), which American Home Products, Inc., markets in the U.S., was invented and developed in the United Kingdom by the Imperial Chemical Industries (ICI) and was approved for marketing in the U.S. in 1967.

Proliferation of Second-Rate Drugs Endangers Public

The overwhelming concentration of R&D on drugs which produce little or no therapeutic gain not only is a waste of scarce economic resources, but it also presents ethical problems: the use of human subjects in testing drugs which are known in advance to be unnecessary and duplicative. These types of drugs, which constitute the vast majority, put human test subjects at risk without offering any benefits to the individual himself or to society, a violation of medical ethics.

As far back as 1961, the renowned pharmacologist Dr. Walter Modell warned: "I take the stand that, as a general principle,

(*New molecular entities (NME) approved prior to 1975 were not assigned therapeutic classification.)

everything that adds to the difficulty in dealing with and understanding drugs also makes drugs more dangerous. Thus, the excessive number of needless drugs constitutes a present danger. We can make the useful drugs both less dangerous and more efficient by weeding out the useless, the ineffective and the duplicates, and by so doing, make it possible for the physician to learn in depth about the potent drugs he will prescribe for his patients. We must add only those new drugs that really add something more than their mere presence....Yet, our present trend of increasing the number of drugs without adding real therapeutic qualities tends to dilute experience to a low and sometimes hazardous level, and makes substantial and unbiased knowledge through teaching and reading even more difficult to acquire." (Drug Industry Antitrust Act Part I, p. 320.)

Most "R&D" is Product Development

In testimony before the Antitrust and Monopoly Subcommittee of the Senate Judiciary Committee in the early '60s, a former medical director of a large drug company stated that some wonderful things have been done by some drug companies, but that many of their activities that are called research by the pharmaceutical industry have no relationship to research. A medical scientist from the University of Wisconsin testified that, "the principal reason why drug companies devote most of their scientific resources to what he regarded as relatively unimportant work is their desire to obtain a patentable derivative of a basic drug which is either not patented or on which the patent is held by others."9/

The Subcommittee's final report concluded that:

"If the drug industry subordinates basic research to minor modifications which hold greater assurance of commercial success, it is merely following the pattern of American industry. The difference, however, is that no other industry approaches drugs in stressing its research activity as the rationale for extraordinary profitmaking."10/

Drug Testing for FDA Approval Major Part of Development

The quality of the drug companies' R&D can, to a large extent, be determined by the quality of its testing drug products for FDA approval. Drug testing is by far the largest component of the drug product development process.11/

FDA is in the best position to judge the quality of this large part of R&D.

Former FDA Commissioners Goddard and Ley publicly expressed their consternation with the way drugs are being tested. In a speech before the Pharmaceutical Manufacturers Association in 1966, Dr. James Goddard, then Commissioner of the FDA, said:

"I have been shocked at the materials that come in.... In addition to the problem of quality, there is the problem of dishonesty in the Investigational New Drug (IND) Stage...." I will admit there are gray areas in the IND situation.

"But, the conscious withholding of unfavorable animal or clinical data is not a gray area matter.

"The deliberate choice of clinical investigators known to be more concerned about industry friendships than in developing good data is not a gray area matter.

"The planting in journals of articles that begin to commercialize what is still an Investigational New Drug is not a gray area matter.

"These actions run counter to the law and the ethics governing the drug industry."

Dr. Herbert Ley, who succeeded Dr. Goddard as FDA Commissioner, stated two years later that, "we have not yet seen the degree of improvement in the quality of clinical data from drug testing which we must have." In a speech before the Educational Conference of the Food and Drug Law Institute in December 1968, Dr. Ley claimed that out of 406 drug-marketing applications received by the FDA in 1967, only 59 were approved.

He said:

> "More than half suffered from deficiencies, in clinical studies and inadequacies in efficacy data and many were so low in quality as to be not approvable."

Dr. Ley amplified his views before the Monopoly Subcommittee of the Senate Small Business Committee on May 27, 1969:

> "The major problem in industry submissions to FDA is still the poor quality of both the basic data and the summaries. The most important single step that industry can take to speed up the processing of new drug applications by FDA—— and to improve the chance of new drug approval——would be to ensure that the data presented in support of efficacy is

true to the statutory requirement of well-controlled studies."

Dr. John Jennings, Assistant to the FDA Commission for Medical Affairs, on September 16, 1970, stated:

"The primary cause of the much touted delay in FDA decision-making is beyond all question the poor quality of the data, particularly that of the clinical investigations submitted to us. Although this has improved in recent years, some sponsors still do not accept that a few well-conducted studies are much more persuasive than a mass of poorly documented case studies or even carefully documented random clinical reports."

The House Subcommittee, Chaired by then-Congressman Fountain and now by Congressman Weiss, have discovered that in case after case, some firms have been guilty of misrepresenting, distorting and even withholding information developed in their testing of drugs which might retard or prevent an approval to market. Injury and death have resulted from such actions. Some of these companies were prosecuted for criminal violation of the law.

Dornvall, manufactured by Wallace and Tiernan, caused many deaths and injuries.

Flexin, a product of McNeill Laboratories, a subsidiary of Johnson and Johnson, is another example of "willfully concealing information in the application to FDA and, according to FDA, resulted in 50 cases of liver damage, including 11 deaths.

Panalba, a fixed ratio combination antibiotic marketed by Upjohn, no longer on the market, was heavily advertised and became one of the most frequently prescribed drugs in this country used by millions of people. The Upjohn Company had studies in its files that showed that this product was an irrational combination and that the benefit to risk ratio was unfavorable. Yet, this information was never submitted to the FDA. The result was that the drug was approved for marketing and was widely prescribed by physicians, although there wasn't a single scientific study that this drug mixture made any therapeutic sense. Material supplied by the FDA to the Monopoly Subcommittee indicated that thousands of persons who took this drug suffered from adverse reactions, including deaths.[12/]

Other examples of drug development which violated the law were Flagyl and Aldactone, both marketed by the G. D. Searle Company. As New York Magazine stated in its May 16, 1977 issue:[13/]

> "--Then, when FDA officials conducted an on-site investigation at Searle's Skokie, Illinois research laboratories, the situation began to appear so appalling that a special task force was assembled to conduct a full scale investigation into all Searle research methods. The task force looked into the research behind several major prescription drugs produced by Searle."

Searle manufactures drugs to treat a large variety of illnesses or conditions.

The New York Magazine article continues:

> "At the heart of FDA's regulatory process is the ability to rely upon the integrity of the basic safety data submitted by sponsors of regulated products," observed the Searle

task force in March 1976. "Our investigation clearly demonstrates that in the G. D. Searle Company we have no basis for such reliance now."

These investigators reported, "We have uncovered serious deficiencies in Searle's operations and practices which undermine the basis for reliance on Searle integrity in conducting high-quality animal research to accurately determine or characterize the topic potential of its products."

In addition, during the eleven-year period 1975 to 1985, the Searle Company did not market a single drug which FDA scientists considered a significant contribution to medical care.[14]

Other examples of drugs which were the result of poor research and which were foisted on the public are as follows:

Eli Lilly's Oraflex was approved for marketing in April 1982 as an antiarthritic drug. It caused at least 33 deaths in the United Kingdom, but the company did not inform the FDA. The result was that, after marketing approval in the U.S., it resulted in 49 deaths and 916 nonfatal injuries. It was removed from the market in August 1984.

Smith, Kline and Beckman's "Selacryn, an antihypertensive, was marketed in early 1980. Important information was withheld from the FDA, which resulted in 36 deaths and more than 500 cases of liver and kidney damage.

Both the Lilly Company and Smith, Kline and Beckman pleaded guilty of criminal violation of the law.

Eli Lilly Company was fined $25,000. Its vice president in charge of this product and who pleaded "no contest" was fined $15,000.

Smith, Kline and Beckman in 1982 was fined $100,000. Three executives, who were indicted, pleaded "no contest" and were put on probation for a year and each one was "fined" 200 hours of community service.

A student who was arrested in a Library of Congress sit-in last year was "fined" 300 hours of community service.

Summary and Conclusions

1. The cost of R&D which the drug industry gives as a reason for the high cost of drugs is fictitious. No detailed evidence is given to support the industry's claims. Only by securing the companies' records through subpoena can we ascertain exactly what kind of research and development is being performed, what items are included, and the price paid for each item.

There is evidence that the claimed R&D costs are vastly exaggerated.

2. The high cost of drugs includes not only the normal cost of bringing the drug to the market, but also a tax to finance, in advance, the research programs of the drug companies. The patient who buys brand-name drugs in most cases pays twice for research and development: once for the drug he is using and once for drugs he may never use. The drug consumer is, therefore, taking the risk, not the stockholders who are, therefore, not entitled to receive profits, since profits are the reward for risk in a private enterprise society.

3. Basic research, the development of new knowledge, constitutes a minor part of R&D.

4. Product development, most of which is testing to gain marketing approval, constitutes the major part of "development."

5. The poor quality of research is evidenced by the fact that the vast majority of drugs coming on the market offer "little or no therapeutic gain." According to medical experts and educators these drugs confuse the physicians and make intelligent prescribing more difficult. Proliferation of such

drugs present a danger to sick people, particularly the elderly who use more drugs than other elements of the population.

In addition to the low quality of their development, misrepresentation of results has occurred too often, resulting in injuries and deaths to our people.

6. It is immoral and in violation of medical ethics to put human beings at risk by using them to test drugs which are duplicative, unnecessary, and add nothing to our ability to treat illnesses. People who are used to test such drugs gain no benefits and neither does society.

Recommendations

One of the most important objectives should be to provide incentives to engage in high quality research and development and make it more difficult to market unnecessary, duplicative, and, in most cases, inferior drugs. We, therefore, recommend consideration for the following measures:

1. Vary the life of drug patents. For example, we might consider twenty-year patents (non-renewable) for drugs considered as therapeutic breakthroughs. Perhaps ten years for those offering modest therapeutic contributions, and three to five years for those drugs offering little or no therapeutic gain.

If we assume that the patent system presents an incentive for R&D, then this kind of a system may provide an incentive for R&D to be directed into the first category.

2. There is no reason to encourage more R&D. There is no evidence that we need more of it. What we need is higher quality R&D.

3. We believe that drug coverage under Medicare with a formulary of medically necessary drugs and utilization review

would be very helpful in reducing drug costs, improving prescribing patterns, and improving the quality of research and development for the following reasons:

a. A formulary of drugs which are considered by medical educators and scientists to be medically necessary and superior would serve as an educational device. Practicing physicians have no way of comparing the relative safety and efficacy of drugs. They are continually assaulted by drug company advertising and promotion. The knowledge that particular drugs have been chosen by medical experts as significant contributions to medical practice would be of great value to physicians.

b. Drug companies, if they wish to get their drugs on the formulary, will be forced to channel their R&D into those kinds of drugs which have a reasonable chance of getting on the formulary. This would also tend to reduce the cost of R&D.

c. The cost of drugs to the elderly would decline because the Government could use competitive bidding on a large scale.

4. To discourage the proliferation of unnecessary, duplicative and second-rate drugs, which constitute the vast majority of drugs on the market, the U.S. Government should encourage counter-advertising by universities. Harvard Medical School has such a program which may serve as a model.

We believe that discouraging the use of such drugs could have a beneficial effect on raising the quality of R&D.

FOOTNOTES

1. Competitive Problems in the Drug Industry--Hearings before the Monopoly Subcommittee of the U.S. Senate Small Business Committee, Part 2 p. 645.

2. Arthur D. Little: Worldwide Pharmaceutical Industry Overview: The Context for Shifting R&D.

3. Administered Prices: Drugs, pp. 120ff. Report by the Committee on the Judiciary, U.S. Senate 1961.

4. Op Cit, p. 129.

5. FDA: New Drug Evaluation Project--Briefing Books, September, 1983, Table V-1.

6. Op Cit: Table II-3.

7. "Prescription Drug Price Increases"--Hearings before the Subcommittee on Health and the Environment. Statement of George De Mott, p. 119.

8. New Drug Evaluation: Statistical Report, March, 1986, Appendix FDA Office of Management.

9. Administered Prices Report, p. 130.

10. Op Cit, p. 131.

11. Ibid.

12. Competitive Problems--Op Cit, Part 12, pp. 5165-66.

13. Article: "Warning: Your Prescription May Be Dangerous To Your Health."

14. New Drug Evaluation--Statistical Report, Appendix.

Mr. **Waxman**. Thank you very much, Mr. Hutton and Mr. Guildroy. I know you have with you Ms. Brown and Mr. Gordon to help in answering any of the questions that we might wish to pose.

You are representing the elderly in this country, and you have indicated to us that the elderly are the ones buying most of the prescription drugs, certainly out of proportion to their numbers in the population, and they are paying for these drugs out of their own pockets because Medicare doesn't pay for it, and they're paying more and more each year for higher drug prices.

What is so unique about the drug industry that makes it different than any other industry? If you have another product and they want to raise their prices, the consumers after awhile can stop paying those increased prices, and therefore the marketplace will cause prices to stabilize in some way, or competition would allow the price to be stable, because if you're out of line with your competition, you're going to lose business.

Why can the drug companies increase their prices every year and get away with it and still maintain the high rate of purchases of drugs and the high rate of profits that they receive?

Mr. Hutton, do you wish to answer this, or Mr. Gordon?

Mr. **Hutton**. I wish I really knew. I'll get my economist to give his answer.

I have never been to a hearing of this type, for example, without masses of flak from the drug industry. They come here, they don't even press one pamphlet on you; they'll give you eight pamphlets. That's what they did with me this morning as I came into the room. And they've got plenty of money to spend all the time.

It's amazing to me that they're able to continue that and plead poverty.

Mr. **Waxman**. Well, let's see if we can get somebody on the panel to tell us what's going on economically.

Ms. Brown, why can the drug companies continue to increase prices without some kind of free market pressures keeping those prices under some kind of restraint?

Ms. **Brown**. We don't really understand it, especially when normal market theory would have, when generic competition is introduced, that the brand name would come down to meet that competition. But in this country, unlike other countries like Canada, the brand product tries to distance itself, probably to show that it's that much better a product, and you get what you pay for in this country, and that kind of idea sells. That coupled with a tremendous amount of money going into advertising and promotion to instill that brand loyalty and to convince people that they would be sacrificing the future cures in this country if the don't pay whatever the company charges.

There's no rhyme or reason to pricing in this country. We say kind of offhandedly that they charge what they do because they can. This is one of the last countries without price controls, and I think the PMA states that, you know, Canada, for example, is one of the few countries with compulsory licensing. Well, they're one of the few countries with compulsory licensing because they're one of the only countries without price controls.

Mr. **Waxman**. How much competition is there? Most of the time you get competition bringing the price into some kind of balance. Is there competition in the pharmaceutical industry?

Mr. Gordon, do you want to respond to that?

Mr. **Gordon**. Well, first of all, I'd like to bring up a couple of subjects with respect to the subject you mention. I believe there is a clear violation of the antitrust laws here with respect first of all to the unethical advertising. There seems to be——

Mr. **Waxman**. Excuse me. I'm going to have to ask you to answer my question, because I have a limited amount of time.

Mr. **Gordon**. OK. There is very little competition in the drug industry, first of all. There is certainly no price competition.

There is competition in advertising. In fact, I recall a statement made by a Hoffmann-La Roche person saying, "We have to raise our prices to meet competition." He means that there is advertising competition.

Number two, there is very high concentration in the drug industry. The relevant market is the therapeutic category, and you will notice, using the FTC guidelines, that if the top four companies have more than 50 percent of the market, that's considered high concentration. So you have high concentration for one thing; you have trademark—the use of trademark to maintain a monopoly beyond the patent period.

Mr. **Waxman**. How about patents? How about the fact that they have a patent over a drug? Does that mean that they have a monopoly over the drug for which they have a patent?

Mr. **Gordon**. If you have a patent, you have a monopoly over the drug; that's correct.

Mr. **Waxman**. If you have a monopoly over a product that people need, you then decide how much they're going to pay.

Mr. **Gordon**. Absolutely. In fact, that's the whole idea of a patent. You can decide what they're going to pay.

Mr. **Waxman**. Now the idea of a patent is to let them have that monopoly, so that will give them incentives for research and development, for innovation, and certainly we want innovation in the pharmaceutical area, because it will mean breakthroughs for lifesaving drugs.

Yet our staff survey indicated that when we looked at the price increases for pharmaceuticals and the increases in research and development we find that we are looking at an overall $4.738 billion in the amount of revenues for the price changes and R&D increases of $1.6 billion. This is a difference of almost better than 3-to-1.

Mr. Guildroy, what do you think is happening? Are they putting this money into R&D, or are they just taking advantage of the fact they have a patent and squeezing the consumers for all that they can get?

Mr. **Guildroy**. Well, we are very skeptical about the situation.

Mr. **Gordon**. I don't think that the committee—certainly we never found out, when I was up on the Hill, exactly what they mean by R&D. In fact, I guarantee you——

Mr. **Waxman**. Well, I'm taking their word for R&D costs.

Mr. **Gordon**. I wouldn't take their word.

Mr. **Waxman**. OK. But I'm even accepting their word for it.

Now at some point there is competition, when there's a generic drug. That means the generic drug is out on the market and competing with a brand-name drug.

What do we find under those circumstances, Ms. Brown? Are we seeing prices drop?

Ms. **Brown**. We're seeing even larger increases, especially right before the drug goes off patent. To put it simply, if you're going to lose half your market share, but you're charging twice as much for the product, then you're still doing OK. And it borders on the criminal when this is happening, when that company still has a monopoly, and there is nowhere else to turn.

"Consumers" is really a misnomer in the drug industry, we feel. Consumers have little or no decisionmaking power. They just get to pay the bills.

Mr. **Waxman**. Well, they do have decisionmaking power when there's a generic drug. So are the prices dropping when they can have a generic?

Ms. **Brown**. Well, in some States, they have that power. In other States, your doctor makes that decision. And if the doctors have been convinced by years of industry detailing that their products are better and that you are really using your money foolishly to pay a few cents less for a generic, then what doctor is going to sacrifice their patient, especially when they're told that the elderly are more vulnerable to this?

There is no scientific evidence for this, of course, and we were hoping that the FDA Bioequivalence Conference would put some of those things to rest.

Mr. **Waxman**. Well, even when we have a generic drug that is available to consumers, the brand-name loyalty ingrained in the physician is such that many of those physicians will continue to prescribe the brand-name drug, and we're seeing the brand-name drugs, even when there's this competition, going up in price, even though the generic drug is going down in price.

Ms. **Brown**. Right. Brands always go up. I mean, Motrin is the only one I think that went down, and that's because it went OTC, and I think dipyridamole, since they did something strange with the regulation, has volunteered to keep their prices the same or maybe drop them a little.

This country is alone in that, and it's clearly a function of they do what they can, and perhaps it's a matter of the administration, too, when they learn that with the current administration, that no one was going to be overseeing this aspect of our health care system, and they just kind of took off.

Mr. **Waxman**. Thank you very much.

Let me move on to other members, because I know they have questions.

Mr. Whittaker.

Mr. **Whittaker**. Thank you, Mr. Chairman.

Mr. Hutton, I'd be curious to know, in your opinion, why you feel there is no difference or why there is no reason to encourage more research and development. I think you made that statement in your written testimony, and it cast an opinion that you didn't feel like any new research and development was really needed to be encouraged in pharmaceutical products.

Mr. Gordon. First of all, we don't know whether we have enough R&D or whether we need any more R&D. If you will look at the records of the Food and Drug Administration—and I have them with me, by the way—most, the vast majority of drugs that get on the market are no good. They offer little or no therapeutic gain. Very few drugs that get on the market are significant drugs.

And as a matter of fact, medical educators have testified before my previous committee, the Monopoly Subcommittee of the Senate Small Business Committee, that the more drugs you have on the market, unless they are important drugs, actually make—that is, bring about worse medical practice. You have very bad medical practice, because doctors cannot become acquainted with all the drugs on the market.

Mr. Whittaker. Mr. Gordon, could I——

Mr. Gordon. So unless R&D actually results in significant therapeutic gains, I would say that the rest of the R&D isn't worth anything.

Mr. Whittaker. Mr. Gordon, could I inquire at what stage and in whose hands is the decision whether a drug is going to be therapeutically valuable or not?

Mr. Gordon. Well, the Food and Drug Administration

Mr. Whittaker. You have to wait until the clinical trials have been completed to find out whether it's going to do any good or not.

Mr. Gordon. That's right. As a matter of fact, there are two decisions by the FDA. One, after the new drug application is approved—you'll notice that in that statement, it refers to new drug applications, and you find that the numbers of important drugs are pretty low.

But then you can also tell when a drug reaches the clinical stage, whether it is going to be important or not.

Mr. Whittaker. Well, from what you just referenced, it almost sounds as though you would be in favor of only one or two manufacturers of a product.

Mr. Gordon. No, that doesn't follow at all.

Mr. Whittaker. And not have competition, bringing on their own product line. A new company creating a drug that would be somewhat comparable to another drug, it has to go through those clinical trials.

And are you suggesting that those are unnecessary procedures and that drug companies should not——

Mr. Gordon. I would advocate that before a drug is approved for marketing, that not only should it be shown to be safe and effective, as required by law, but that it's relatively better or at least as good as a drug that is already on the market. If it's as good that would be fine. But if it doesn't meet the previous standards, I don't think it should be allowed on the market.

In fact, this stand was advocated by Dr. James Goddard, when he was a Food and Drug Commissioner.

Mr. Whittaker. You know, I can appreciate what you're saying. But in a free market situation, that would be suggesting that the Consumer Product Safety Commission could disallow Korean automobiles, because they were deemed to not be quite as satisfactory as a German automobile.

Mr. GORDON. What do you mean by "free market?" You mean—a consumer isn't able to select the drug that he wants. He can't compare. There's not as free a market as you say there is.

Mr. WHITTAKER. I'm just curious, Mr. Gordon. If you feel like that the primary problem is maybe with the doctor's prerogative of making a prescription choice—we're talking a great deal about the consumer's choice, and though he is dependent upon his physician to make that prescription recommendation, isn't your primary argument against allowing that physician to have the prerogative to make a choice for his patient?

Mr. GORDON. No, not at all. As a matter of fact, I'm in favor of making sure that he gets some objective information, which he very seldom gets right now. He's assaulted by advertising and promotion. Pfizer comes in to you, if you're a doctor, and says, "My drug is better." Somebody else comes in and says, "My drug is better." The doctor is in no position to make such a decision.

As a matter of fact, the Task Force on Prescription Drugs, which was a panel set up by Secretary of Health, Education, and Welfare, John Gardiner, which consisted of some of the outstanding educators and medical scientists in this country, came up with a rather interesting conclusion, that doctors know very little about drugs. And Dr. Krogh, Richard Krogh, testifying before my committee said that he fears for the future of his chosen profession, because the industry has practically taken over post-graduate medical education.

Well, the doctor is in really no position to make a decision.

Mr. WHITTAKER. Let me ask a further question, Mr. Gordon.

Mr. GORDON. Sure.

Mr. WHITTAKER. I had other questions for other panelists, but I'm just curious. If you feel like that the doctors' professional judgment is so weak in the area of brand selection, who would you direct to have authority over your physician to direct to him what he could prescribe and what he could not?

Mr. GORDON. Well, as I stated, I would like to see some medical education.

Mr. WHITTAKER. From where? Are you saying that the FDA should tell the doctor, you can prescribe one, two or three items but disregard the other eight below the list?

Mr. GORDON. I would say that the government should perhaps put out a compendium. I would say that medical schools like Harvard Medical School has detail men to go out and educate doctors. There are many ways to do it, by the way. This is from the task force——

Mr. WHITTAKER. Provided it is not too long. Maybe we can just enter it into the record.

For the sake of discussion, I think we can probably conclude and I know my time has expired, but I am somewhat concerned with the disparaging remarks that you made concerning the physician's ability to intelligently choose a prescription drug for his patient.

Mr. GORDON. I'm surprised that you are not aware of the fact that doctors don't know much about drugs, they are really not expert in selecting drugs.

Mr. WHITTAKER. I would welcome a further panel that would maybe give some balance to that perception of yours.

Mr. HUTTON. Maybe, Mr. Whittaker——

Mr. WAXMAN. Mr. Hutton, I am going to interrupt because the gentleman's time has expired. Maybe we can have that as a topic for another hearing. Mr. Wyden reminds me that on Wednesday, we are going to have a hearing somewhat on that subject when it comes to the question of physicians prescribing drugs and making a profit, which is an issue that is a bit off the target of the main focus of what we want to talk about today.

Mr. Sikorski.

Mr. SIKORSKI. Mr. Chairman, in the interest of time, I'll defer my questions. I thank the panel for coming.

Mr. WAXMAN. Thank you. Mr. Wyden.

Mr. WYDEN. Thank you, Mr. Chairman.

Mr. Guildroy, I was director of the Gray Panthers for many years before I came to the Congress and I'm particularly concerned about how these high prices affect senior citizens. There are a number of executives from the big pharmaceutical manufacturers in this country in the room right now. You have an ideal chance to communicate directly to these firms about the big increases that your members are paying.

Could you tell us what these big increases mean for senior citizens in terms of them having to give up food or paying the rent or the utility bills? What does it really mean in human terms for senior citizens?

Mr. GUILDROY. Mr. Wyden, I'd like to defer to Ms. Brown, please.

Ms. BROWN. We did a survey, I know it has been thrown around a lot that people are foregoing food and rent for drugs, but we actually did a survey to measure the impact of the high drug costs. We did it in 1985 and 1986. We also did one in 1982. One thing we found was that in reasons for deciding not to get a prescription filled, in 1982, cost was the fourth reason. Now, it's the second reason for deciding not to get a prescription filled. We don't know what that does to the more costly services of physician visits or perhaps hospitalizations that people are foregoing necessary drug therapy.

The survey also showed that in 1 year alone, between 1985 and 1986, there was a 42 percent jump in the amount of people who were paying the highest amount that we asked for in their prescription drugs out of pocket. It was a range that they could answer, what are you paying out of pocket and the highest category was, I am paying over $40 a month, which is nearly $500 a year.

We can't get a per capita figure on that unfortunately because that person paying over $40 a month could be paying $41 or $400. We don't know.

We have actually got some data to support some of the more emotional arguments that have been made in the past.

Mr. WYDEN. One last question if I might, Mr. Guildroy. Because you run the AARP Pharmacy, has it been your experience that the price of generic drugs is not going up quite as fast as the price of brand name drugs?

Ms. BROWN. The price of generics either remains steady or drops. Generics compete on price. The brand names certainly don't. We see no increase in generics. That might even be pulling the CPI down, if you have more generics on the market that actually underestimates the even greater inflation in the prices of the brand names.

Mr. WYDEN. Mr. Chairman, I do not have any further questions but I think this is one of the critical issues for this subcommittee's consideration. Obviously, the generic drugs on the basis of their programs are not going up at the rate of the brand names. Clearly there seem to be some competitive forces at work with the generic drugs that are not available in some of the other markets. I would hope that would be an issue we would talk about later.

Mr. WAXMAN. Will the gentleman yield to me?

Mr. WYDEN. I'd be happy to yield.

Mr. WAXMAN. On the question of the generic drugs, we have seen increases in R&D expenses, not as high as the price increases, but we have also seen increases in the amount of money to promote, advertise and to otherwise encourage people to buy these brand name products. The great part of that has been an anti-generic campaign where the brand name companies, in order to hold on to their share of the market, are trying to disparage generic drugs and saying they are not as good, they are not as bioequivalent, they are not as effective and they are not as safe.

We know that's not true because the FDA has testified and will testify again today, that is absolutely not true. A generic couldn't be approved unless it were the same drug and met all the standards for safety and efficacy.

How do your members feel? I know the AARP sells drugs, both brand names and generic drugs. How would your members feel if they found out they are paying higher prices for drugs so they could be discouraged from buying drugs that would be less costly to them?

Ms. BROWN. We find our members are responding in a way that they have been told that generic drugs are like generic corn flakes, they are awful. We have survey data also to show that between 1985 and 1986, there was 10 percentage points that shifted in the answer to a question, do you think the FDA holds the same standards for quality, safety and effectiveness for generics as brand, and they shifted, in 1985, they said, yes, we do. In 1986, 10 percent jumped right into the "don't know" category. That's a 42 percent increase in the amount of people who are now confused and indeed don't know.

No one is going to buy a product if there is a doubt. It certainly is not worth a few dollars more. They are absolutely right. They are very effective in those campaigns.

Mr. WAXMAN. This expenditure by the pharmaceutical industry to deceive people is effective and it is also adding to their profits because they can go ahead and charge prices because they maintain their monopoly?

Ms. BROWN. Absolutely; it's adding insult to injury.

Mr. WAXMAN. Thank you very much.

Mr. WYDEN. Thank you, Mr. Chairman.

Mr. WAXMAN. Mr. Coats.

Mr. COATS. Thank you, Mr. Chairman. I don't know that I have specific questions but I do want to make a comment and maybe some of the panelists would like to respond.

I can appreciate as all of us can that we represent senior citizens and that they are an important part of our constituency. We all have parents that are older, and we are sensitive to the costs of drugs, generic, prescription, over the counter, whatever. The incidence of medical costs on senior citizens are higher in most cases than the general public.

I guess the question I have is while we recognize that some drugs are expensive, most drugs are expensive, we also recognize how important they are to our well being, how critical they are to senior citizens' health and to maintaining that health in older years. I now have a father that is 81 years old who has Parkinson's and a number of other medical problems, so our drug bills are fairly steep. Yet he lived and spent his career working for an ethical drug company, distributing drugs and in the sales force and also involved, in a minor degree, in research of drugs.

I grew up with some understanding of what it takes to research and develop, find a drug that can bring about medical relief, what it takes to get that drug approved by the FDA. Often times, it's millions of dollars and years and years of research and clinical testing before a drug is approved. This results in a cost for a drug that people, on the surface look at and say, why should that drug cost so much, without focusing on a decade of research and development, a decade of bureaucratic process in getting it approved, and a decade of clinical trials.

I wouldn't want it overlooked by the panel or by those focusing on this hearing, that what we are looking at here is a situation in which number one, cost recovery is significant but number two, incentive has to remain for drug companies to develop these drugs, of which many of our senior citizens now take advantage and say, what a wonderful miracle drug this is, why does it cost $1 instead of $0.09?

If you remove that incentive, those miracle wonder drugs may not be there because who is going to spend the amount of money and the amount of research necessary to develop those drugs.

I see, Ms. Brown, that you would like to respond.

Ms. BROWN. I would like to respond. Thank you.

I think that what we are talking about is a matter of degree only. AARP would be the last organization to throw any disincentive to develop new cures for the illnesses that so often plague our members and the population at large.

We differ a little from our co-panelists here in that we do think that important therapeutic gains aren't made in leaps and bounds, that often they are made in increments and yes, we kind of do owe them a living. Also, we acknowledge that the successful drugs must also pay for the failures, the ones that died with the bench scientist.

However, it's a matter of degree. It's a matter of looking at who is paying for this, not only who is paying for the R&D which I personally would like to see spread out over the tax base, but who is paying for all the rest of the profits and activities of the pharmaceutical industry, which is by definition sick people, maybe excluding those taking birth control pills or something, you are talking about sick people who are supporting it.

Mr. COATS. Who should pay?

Ms. **Brown**. Who should pay?

Mr. **Coats**. Should those that are healthy pay?

Ms. **Brown**. There but by the grace of God go all of us.

Mr. **Coats**. Are you advocating that we spread all these costs over the general public?

Ms. **Brown**. I would like to see there be reasonable returns and reasonable profits because that's our system and that——

Mr. **Coats**. Who determines what is reasonable?

Ms. **Brown**. Certainly not the drug companies.

Mr. **Coats**. Who then?

Ms. **Brown**. I suppose I would be over stepping our testimony to engage in some kind of rate review board, so I will defer on that, although that is something we could discuss on Thursday's drugs under Medicare hearing, where we will be testifying with Mr. Stark, and talking about some cost containment mechanisms and financing.

Mr. **Coats**. Is anyone advocating we remove the prescription drugs and remove drug pricing from the marketplace and establish a Government commission?

Ms. **Brown**. I'm sure lots of people are going to be proposing that.

Mr. **Coats**. Do you see that as having any possible disincentive toward the production of new drugs, research and development of new drugs?

Ms. **Brown**. I guess it depends on what your return is. It's a matter of if the profits are so great in the drug industry and that is supporting R&D but R&D is only 10 to at the outside 15 percent of your budget, what else are you supporting? You are supporting corporate jets. You are supporting conferences in the Bahamas. You are supporting a whole lot of extraneous stuff that doesn't necessarily have to do with R&D and all of the things that we pay homage to.

Mr. **Coats**. What you are advocating sounds to me like a radical departure from a system that has probably brought more drug breakthroughs, a better level of medicine than any other nation in the world.

Ms. **Brown**. The industry has given us a lot but also it's not all the breakthroughs that are here. There are some other countries that develop the drugs and then we license them in. It's not just that America has the only scientists that can develop these products. There are a lot of breakthroughs coming out of universities. They don't have this almighty profit incentive. There are research scientists.

AZT came out of a Government funded program.

Mr. **Coats**. Do you really think we would be better off under a government funded, Government directed program, that we would have a better level of medicine, that we would have more research, more drugs coming into the market?

Mr. **Waxman**. The gentleman's time has expired.

Ms. **Brown**. I don't feel comfortable answering that question the way it is framed. It is kind of like if you stop beating your wife. I don't like the way it would make me answer.

Mr. **Coats**. You are proposing one system. I was advocating that the present system has probably given us a better level——

Ms. **Brown**. We would like to restructure the present system, not throw it out, restructure it.

Mr. **Waxman**. Thank you, Mr. Coats.

I want to thank the witnesses that have testified before us this morning. You have been helpful in giving us your preliminary information. We look forward to working with you.

Our next panel is Mr. Gerald J. Mossinghoff, president of the Pharmaceutical Manufacturers Association; Mr. Douglas G. Watson, president, Pharmaceuticals Division, Ciba-Geigy Corporation; Mr. Donald E. O'Neill, executive vice president, Warner-Lambert Company; Mr. Paul N. Clark, president, Pharmaceutical Products Division, Abbott Laboratories; and Mr. Harry Shoff, president, Winthrop Pharmaceuticals, Sterling Drug, Inc.

We are pleased to welcome you to our subcommittee hearing this morning. Your prepared statements will be part of the record in full. What we would ask of each of you is to summarize or give us your presentation as you see fit, but to try to keep that presentation to 5 minutes.

Mr. Mossinghoff, why don't we start with you?

STATEMENTS OF GERALD J. MOSSINGHOFF, PRESIDENT, PHARMACEUTICAL MANUFACTURERS ASSOCIATION; DOUGLAS G. WATSON, PRESIDENT, PHARMACEUTICALS DIVISION, CIBA-GEIGY CORP.; DONALD E. O'NEILL, EXECUTIVE VICE PRESIDENT, WARNER-LAMBERT CO.; PAUL N. CLARK, PRESIDENT, PHARMACEUTICAL PRODUCTS DIVISION, ABBOTT LABORATORIES; AND HARRY SHOFF, PRESI[illegible], WINTHROP PHARMACEUTICALS, STERLING DRUG, INC.

Mr. **Mossinghoff**. Thank you, Mr. Chairman.

Mr. Chairman, with your permission, I would like to use 5 graphics, if I could, to support the summary points I will make during this 5-minute presentation.

Mr. **Waxman**. Certainly. Present them as you see fit.

Mr. **Mossinghoff**. Mr. Chairman, in the summary portion of my statement, I would like to make nine points.

First is that our way of life in the United States would be unimaginable without the modern medicines discovered and developed by the PMA companies through their research and development. During 1986, PMS companies invested $4.6 billion in research and development, an increase of 12 percent over 1985. People are living longer, healthier, and more productive lives as a direct result of that investment.

Second, in recent years, the cost of providing health care and the prices charged have risen substantially. The same is true for prescription drugs. But modern prescription drugs are a very good value. Prescription drug prices have remained well below the overall Consumer Price Index ever since that index was defined as 100 in 1967, and drug prices today are less than two-thirds the overall price index for medical care.

That is shown on figure 1 of my chart. The differences, Mr. Chairman, between your chart and my chart is that yours is a rate of change chart, and obviously as a policymaker, the Congress must look at that very carefully. My chart plots dollars, and the fact is that people walking into a drugstore spend less today buying prescription drugs than they do if they walk into another store and buy the other items that are tracked in the Consumer Price Index.

Prescription drugs and related products sold in retail pharmacies were half of the 1960 level as a percentage of health care cost, and that's shown in figure 2 that is being exhibited. In 1967, a typical worker had to work 1 hour and 20 minutes to pay for an average prescription. By 1985, it took only 63 minutes for that same prescription.

Third, modern medicines not only save lives, prevent disease, and cure illness; they also save billions of dollars each year by reducing the need for surgery, hospitalization, and other more expensive forms of therapy. In its first 10 years, the anti-ulcer drug, Tagamet, saved $4 billion in the United States alone. Other examples are discussed in my full statement.

Fourth, research and development are the hallmarks of the PMA companies. Their investment in R&D continues to double every 5 years, as shown in figure 3. Moreover, the industry is investing an increasingly higher percentage of sales, currently 15 percent, to finance its growing investment in research and development, and that's shown in figure 4.

Measuring increases in R&D expenditures the same way we measure price indexes and price increases, the index for research and development conducted by PMA now stands at well over 1000, 3⅓ times the prescription drug Consumer Price Index.

Fifth, the period of time during which this enormous investment in research and development can be recovered through sales revenues is being dramatically compressed due to a number of converging forces. Foremost is the unprecedented surge in competition from generic products as soon as the patent on the pioneer product expires. Other major forces include the intense competition within the research-based pharmaceutical industry to develop and market new patented drugs, the increasing delays in the approval of new drugs by the Food and Drug Administration and increasing foreign competition from developed countries that have targeted this industry and from newly industrialized countries that blatantly condone patent piracy.

Sixth, nevertheless our companies so far remain competitive in world markets. The U.S. pharmaceutical industry, despite its relatively small size, ranks 4th among the 10 leading high-technology industries in contributing a positive trade balance. In 1986, for the first time, those 10 industries had a net negative balance of trade totaling $2.6 billion, but pharmaceuticals contributed a positive balance of $764 million.

But our industry's leadership position in world markets is not assured. From 1976 through 1980, the U.S. pharmaceutical industry contributed 70 new drugs to world markets, more than one-fourth of the total and twice the number originating from Japan. In sharp distinction, during the last 5 years, Japan introduced 60 new drugs in the world markets as compared with 58 originating from the United States.

Seventh, Congress can and should take several important steps to help restrain the forces tending to drive up prices of modern medicines. These include appropriating the funds necessary to streamline the new drug approval process at the Food and Drug Administration; continuing to encourage other countries to strengthen the protection of patents and trademarks; protecting U.S. process patents from foreign pirates; reforming our chaotic product liability system; and strengthening the tax incentives for research and development.

Later in my prepared statement, I cite specific bills that the PMA supports to carry out those reforms.

Eighth, strong patent protection worldwide is essential to the pharmaceutical industry's continued investment in research and development. PMA welcomes the steps being taken by some of our trading partners to strengthen patent protection for pharmaceuticals. These steps include the Japanese Government's decision to seek enactment of patent term restoration legislation for pharmaceuticals, the active consideration within the European Community of a similar measure, the new protection in Korea for pharmaceutical products, and a parliamentary consideration in the United Kingdom to repeal the so-called "license of right."

Mr. Chairman, let me go to my last point in the interest of time. The research-based pharmaceutical industry stands on the threshold of a Golden Age of development. New and exciting knowledge about molecular biology and new methods of research and development, including computer modeling of molecules and cells and advances in biotechnology, will enable PMA companies to develop new treatments and cures for such deadly diseases as cancer, heart disease, Alzheimer's disease, leukemia, and AIDS. These dreams, however, will become a reality only if the incentives remain for the research-based pharmaceutical industry to continue its enormous investment in research and development.

Thank you very much, Mr. Chairman.

[Testimony resumes on p. 284.]

[Mr. Mossinghoff's prepared statement follows:]

Statement

Pharmaceutical
Manufacturers
Association

GERALD J. MOSSINGHOFF
PRESIDENT, PHARMACEUTICAL MANUFACTURERS ASSOCIATION

BEFORE THE

SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT
COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES

APRIL 21, 1987

Mr. Chairman and Members of the Subcommittee:

I am Gerald J. Mossinghoff, President of the Pharmaceutical Manufacturers Association. PMA represents more than 100 research-based pharmaceutical companies that discover, develop and produce most of the prescription medicines used in the United States. I appreciate this opportunity to appear before the Subcommittee and testify on the important subject of prescription-drug prices.

SUMMARY

Mr. Chairman, with the help of graphics and as developed more completely in the remainder of this statement, I would like to make the following points in this brief summary:

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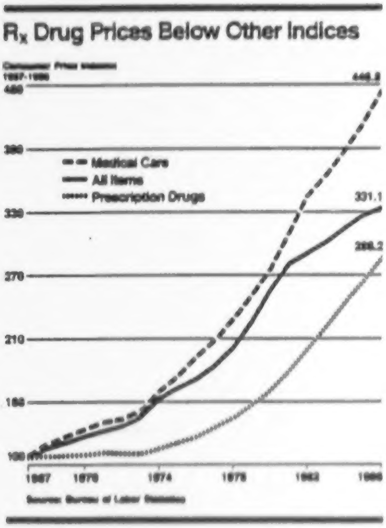
(1) Our way of life in the United States would be unimaginable without the modern medicines discovered and developed by the PMA companies through their research and development. During 1986, PMA companies invested $4.6 billion in R&D, an increase of 12% over 1985. People are living longer, healthier and more productive lives as a direct result of that investment.

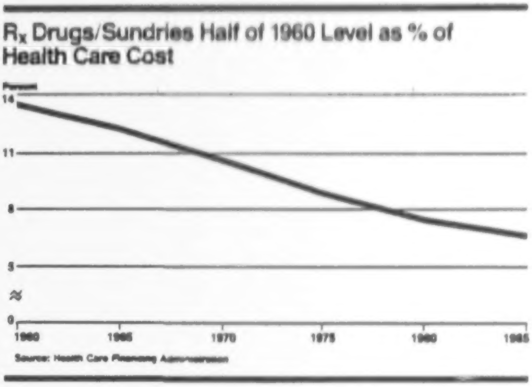
(2) In recent years, the costs of providing health care, and the prices charged, have risen substantially. The same is true for prescription drugs. But modern prescription drugs are a very good value. Prescription-drug prices have remained well below the overall Consumer Price Index ever since that index was set at 100 in 1967. And drug prices today are less than two-thirds the overall price index for medical care (Figure 1). Prescription drugs and related products sold in retail pharmacies in 1985 were half of the 1960 level as a percentage of health care costs (Figure 2). In 1967, a typical worker had to work one hour and twenty minutes to pay for an average prescription; by 1985, it took only 63 minutes to pay for that prescription.



R_x Drug Prices Below Other Indices

Source: Bureau of Labor Statistics

Figure 1



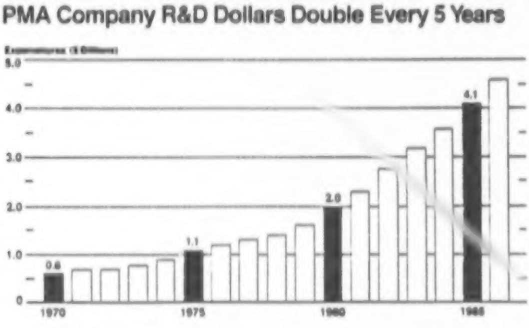
R_x Drugs/Sundries Half of 1960 Level as % of Health Care Cost

Source: Health Care Financing Administration

Figure 2

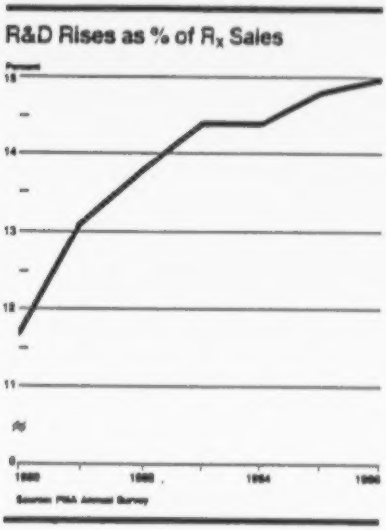
(3) Modern medicines not only save lives, prevent disease and cure illness, they also save billions of dollars each year by reducing the need for surgery, hospitalization and other more expensive forms of therapy. In its first 10 years, the anti-ulcer drug Tagamet saved $4 billion in the United States alone. Other examples are discussed later in my statement.

(4) Research and development are the hallmarks of the PMA member companies. Their investment in R&D continues to double every five years (Figure 3). Moreover, the industry is investing an increasingly higher percentage of sales--currently 15%--to finance its growing investment in R&D (Figure 4). Measuring increases in R&D expenditures the same way we measure price increases, the "index" for R&D conducted by PMA companies now stands at over 1,000, three and one-half times the prescription drug CPI (Figure 5).



Source: PMA Annual Survey

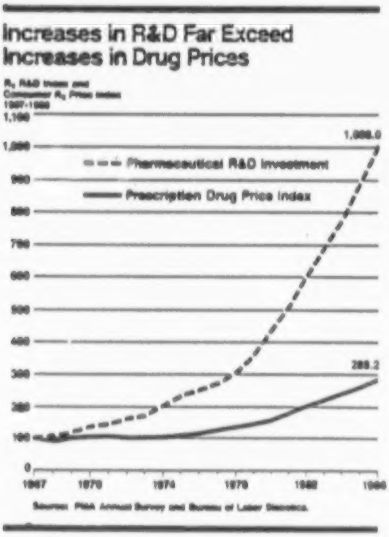
Figure 3



R&D Rises as % of R_x Sales

Source: PMA Annual Survey

Figure 4



Increases in R&D Far Exceed Increases in Drug Prices

Source: PMA Annual Survey and Bureau of Labor Statistics.

Figure 5

(5) The period of time during which this enormous investment in R&D can be recovered through sales revenues is being dramatically compressed due to a number of converging forces. Foremost is the unprecedented surge in competition from generic products as soon as the patent on the pioneer drug expires. Other major forces include the intense competition within the research-based pharmaceutical industry to develop and market new patented drugs; increasing delays in the approval of new drugs; and increasing foreign competition from developed countries that have targeted this industry and from newly industrialized countries that blatantly condone patent piracy.

(6) Nevertheless, our companies so far remain competitive in world markets. The U.S. pharmaceutical industry, despite its relatively small size, ranks fourth among the ten leading high-technology industries in contributing a positive trade balance. In 1986, for the first time, those ten industries had a net negative balance of trade, totaling $2.6 billion, but pharmaceuticals contributed a positive balance of $764 million. But our industry's leadership position in world markets is not assured. From 1976 through 1980, the U.S. pharmaceutical industry contributed 70 new drugs to world markets, more than one-fourth of the

total and twice the number originating from Japan. In sharp distinction, during the last five years, Japan introduced 60 new drugs into world markets as compared with 58 originating from the United States.

(7) Congress can--and should--take several important steps to help restrain the forces tending to drive up prices of modern medicines. These include appropriating the funds necessary to streamline the new-drug approval process at the Food and Drug Administration; continuing to encourage other countries to strengthen the protection of patents and trademarks; protecting U.S. process patents from foreign pirates; reforming our chaotic product-liability system; and strengthening the tax incentives for research and development. Later in this statement I cite specific bills that should be passed to accomplish these goals.

(8) Strong patent protection worldwide is essential to the pharmaceutical industry's continued investment in research and development. PMA welcomes the steps being taken by some of our trading partners to strengthen patent protection for pharmaceuticals. These steps include the Japanese Government's decision to seek enactment of patent term restoration legislation for pharmaceuticals; the active consideration within the European Community of similar legislation; the new

protection in Korea for pharmaceutical products; and the parliamentary consideration in the United Kingdom to repeal the so-called "license of right"--a compulsory licensing provision during the last four years of a U.K. patent--insofar as that license of right applies to pharmaceuticals. We also view as significant the decision of the Canadian Government to seek modification of the Canadian compulsory licensing provisions, although even with the changes proposed, the Canadian protection of pharmaceuticals will still fall far short of that provided in all other developed countries. There are, of course, many countries in the world which foster the theft of U.S. research and development by failing to provide adequate patent protection. PMA welcomes the efforts of the Executive Branch and the Congress in demanding adequate protection for intellectual property as a critical element of U.S. trade policy. The efforts of Chairman Dingell and the Committee on Energy and Commerce have been most helpful in this area.

(9) The research-based pharmaceutical industry stands on the threshold of a golden age of development. New and exciting knowledge about molecular biology, and new methods of research and development--including computer modeling of molecules and cells and advances in biotechnology--will enable PMA companies to develop new

treatments and cures for such deadly diseases as cancer, heart disease, Alzheimer's disease, leukemia and AIDS. These dreams will become a reality only if incentives remain for the research-based pharmaceutical industry to continue its enormous investment in research and development.

Mr. Chairman, this concludes the summary portion of my statement. The points I have made are developed more fully in the rest of my statement.

STATEMENT

People in the United States are living longer, healthier and more productive lives as a direct result of the new drugs developed by PMA member companies.

In addition to helping to improve health, medicines traditionally have been a bargain for consumers. Even though they are the most cost-effective form of therapy, they have consumed a declining share of health-care expenditures. Over the years, the Consumer Price Index has increased much more than prescription-drug prices. During the 19-year period from 1967 (which the U.S. Bureau of Labor Statistics uses as a base year in calculating the Consumer Price Index) through 1986, the rate of inflation exceeded prescription-drug price increases by 20%. And drug prices today are less than two-thirds the overall price index for medical care.

Meanwhile, prescription drugs and related products sold in retail pharmacies have declined as a percentage of national health expenditures. In 1960, we spent 13.6% of total health-care expenditures on drugs and related products; by 1985, the latest year for which complete data are available, we had cut that share by more than half, to 6.7%. Indeed, we spend less than a nickel of each health-care dollar for prescription drugs from retail pharmacies. The cost of prescription drugs also has declined in terms of purchasing power. Twenty years ago, a typical worker had to work one hour and twenty minutes to pay for an average prescription; by 1985, it took only 63 minutes to pay for that prescription.

Besides saving lives and preventing disease, modern medicines represent the most cost-effective form of therapy. They are an important part of the solution to helping restrain health-care costs: they save billions of dollars a year by reducing the need for alternative, more expensive forms of therapy. "Prescription drug products help contain the total cost of health care by reducing hospitalization and need for surgery," the Department of Commerce's 1987 U.S. Industrial Outlook stated. The use of drugs also reduces physicians' expenses and the number of work days lost due to illness.

The cost-effectiveness of prescription drugs has been well documented. In the 10 years after its introduction in 1976, the anti-ulcer drug Tagamet is estimated to have reduced costs associated with ulcer disease--including work loss and allowing for the cost of the drug--by $5.8 billion worldwide. Savings in the United States alone were $4 billion.

A series of studies sponsored by PMA provides other examples of the cost-effectiveness of prescription drugs. The net annual benefits of using beta blockers--a class of cardiovascular drugs--to prevent second heart attacks was found to range from $1.6 billion to $3 billion. A study of a measles vaccine determined that benefits were more than 10 times the costs over a nine-year period. Treating mental patients with an anti-psychotic drug was found to be the least costly of five forms of therapy--lower by 26% to 62%--and to be one of the most effective methods.

Further, there has been a trend--which is accelerating --to develop drugs that last longer than alternative therapies and thus require fewer doses a day or a shorter course of treatment. The cost of treatment with these new medicines often is considerably less than with older alternatives. One example of this trend was documented in a study, published in the November-December 1984 Reviews of Infectious Diseases, of a new cephalosporin antibiotic that can be administered once a day, rather than three or four times daily as required for conventional cephalosporins. Estimated annual savings from the use of this new once-a-day drug instead of older alternatives ranged from $85 million to $115 million.

Our industry is increasing its efforts to develop new and better medicines. "There is perhaps no industry that depends as heavily on new products--and thus on research and development --as does pharmaceuticals," according to the February 23, 1987 edition of Forbes. Every five years since 1970, our industry has doubled its R&D expenditures. This trend continued in 1986, when the industry spent a record $4.6 billion on research and development, an increase of 12% over 1985. By comparison, the National Institutes of Health estimates it spent $5 billion in 1986 on all health research.

To finance this research and development, our companies have used an increasingly larger proportion of U.S. sales revenues. From 1973 to 1980, the U.S. research-based pharmaceutical industry invested between 11.1% and 11.7% of U.S. sales in R&D. In 1981, the industry increased its investment to 13.1% of sales, and in 1986 our companies invested an estimated 15% of sales in research and development. Measuring increases in R&D expenditures the same way we measure price increases, the "index" for R&D conducted by PMA companies now stands at 1,008, three and one-half times the prescription-drug CPI.

The time during which this enormous investment in R&D can be recovered through sales revenues is being dramatically compressed due to a number of converging forces. Foremost is the unprecedented surge in competition from generic products as soon as the patent on the pioneer drug expires. Since enactment of the Drug Price Competition and Patent Term Restoration Act in 1984, 659 Abbreviated New Drug Applications (ANDAs) to market generic products were approved by the Food and Drug Administration through 1986. Other major forces include the intense competition within the research-based pharmaceutical industry to develop and market new patented drugs; increasing delays in the approval of new drugs; and increasing foreign competition from developed countries that have targeted this industry and from newly industrialized countries that blatantly condone patent piracy.

Ours is a highly competitive industry in which no company commands more than 7% of total sales and the top 20 companies have less than 75% of sales. Our companies compete with each other by striving--with all their resources and scientific ingenuity--to develop better treatments and cures. In this constant quest, thousands of compounds are screened and analyzed for each new chemical entity that eventually is brought to market.

Our industry is competitive in world markets. Despite its relatively small size, the pharmaceutical industry ranked fourth (behind the aircraft, plastics and office machinery industries) in contributing a positive balance of trade among the ten high-technology industries tracked by the Commerce Department. Our industry recorded a postive balance of trade of $764 million in 1986, a year when the ten high-technology industries as a whole had a negative balance for the first time, of $2.6 billion.

Our industry, nevertheless, is facing increasing competition from foreign companies. From 1976 through 1980, for example, the U.S. pharmaceutical industry introduced 70 new drugs in world markets, more than one-fourth of the total and twice the number introduced by Japanese companies. In the last five years, however, Japanese firms introduced 60 new drugs in world markets compared to 58 introduced by American manufacturers.

There are important steps that Congress can--and should--take that would help to stimulate research, improve the competitive position of our industry in world markets and limit the upward pressure on drug prices.

First of all, Congress should strongly support Commissioner Frank E. Young's efforts to improve operations at the Food and Drug Administration and thus streamline the FDA's new-drug approval process. This can be done by fully funding the Fiscal Year 1988 budget request, and by directing additional resources to the drug-approval effort to support Dr. Young's Action Plan.

Quite properly, the FDA gives top priority to ensuring that new drugs are shown to be safe and effective before it approves New Drug Applications and allows new drugs to be marketed. But unnecessarily long periods of review can deprive patients of new, effective medicines.

Despite the very dedicated and able efforts of Commissioner Young and his staff, it still takes much too long to approve new drugs. The average development time for the 20 new drugs approved by FDA in 1986 was more than 10 years from discovery to approval. The mean approval time for those drugs--that is, from the time the application for approval was filed until the FDA completed its review and approved the drug--was 34.2 months. Fifteen of the 20 new drugs had already been approved first abroad; the countries that approved them first did so in an average of 10 months--less than one-third of the FDA's 34-month review time.

Streamlining the approval process would reduce the cost of pharmaceutical research and development, and exert a moderating influence on the powerful push toward higher development costs and thus higher prices. Professors Henry Grabowski and John Vernon, economists at Duke University, found in a study published in 1982 that a reduction of a year and a half in the FDA's approval time would enable companies to recover their research and development costs a full five years earlier.

The average cost of developing a new drug now is about $113 million. This figure is based on a study performed by Dr. Ronald Hansen, then with the University of Rochester School of Management, of the cost of developing a new drug in 1976, updated in accordance with the National Institutes of Health biomedical deflator.

Pharmaceutical research is becoming increasingly expensive in part because the nature of the work is changing in a fundamental way. In the past, pharmaceutical companies engaged primarily in "applied" research, greatly relying on the "basic" research conducted by university scientists, the NIH and other researchers. In recent years, company scientists increasingly have been conducting their own basic research to understand how life and disease function at the cell level, in order to attack disease at its roots rather than simply treat its symptoms. This kind of research on the frontiers of medical science is much more complicated and expensive than the earlier kind of pharmaceutical research.

Moreover, drug companies now are concentrating more on chronic and degenerative diseases such as cardiovascular disease and cancer rather than on infectious diseases. Research on cardiovascular drugs, for example, increased from 14.9% of total U.S. research and development in 1975 to 26% in 1985, while research on drugs to treat cancer and related diseases increased from 15.5% to 18.1% during the same period.

Chronic diseases are treated over longer periods of time than infectious diseases, which increases both the difficulty of assessing drug efficacy and the chances of undesirable side effects. This makes it much harder--and more expensive--to conduct adequate clinical trials for the increasing number of drugs being developed to treat chronic and degenerative diseases. Clinical testing now requires more funds than any other aspect of pharmaceutical research--21% of total research expenditures in 1985.

In addition to supporting efforts to streamline the FDA's new-drug approval process, Congress should move to strengthen the power of the United States Trade Representative by enacting strong intellectual-property provisions in pending trade legislation. Provisions such as those in the Trade and International Economic Policy Reform Act of 1987 (H.R. 3), which is awaiting floor action, would help to persuade our trading partners to provide adequate intellectual property protection. Among many other things, the legislation would modify Section 301 of the Trade Act of 1974 (as amended), which authorizes the President to retaliate against unfair barriers to U.S. trade and investment, and would require the USTR to initiate negotiations with countries that fail to provide adequate intellectual property protection.

Each year, our companies lose hundreds of millions of dollars in sales to products made by patent pirates in countries that blatantly condone such action by failing to provide adequate protection. We have identified 25 countries that do not provide such protection and, in a survey of just five of these countries, sales by U.S. companies of patented products amounted to $162 million in one year--compared to sales by patent pirates of $192 million.

We are encouraged by what we hope is an international trend toward stronger protection for pharmaceutical inventions. For example, the Japanese Government has decided to seek legislation providing for patent-term restoration for pharmaceuticals. The European Community is considering similar legislation. Korea now has agreed to provide product patent protection for pharmaceuticals. In the United Kingdom, Parliament is moving toward repealing a compulsory licensing provision that applies during the last four years of a pharmaceutical patent in that country.

In addition, the Canadian Government has made a major decision to urge enactment of legislation to modify that country's compulsory-licensing provisions. We view that as a significant step. Passage of the legislation would be an improvement over the existing situation, but, even with the proposed changes, patent protection for drugs in Canada would still fall far short of that provided in all other developed countries. The efforts of Chairman Dingell and the Committee on Energy and Commerce have been most helpful in encouraging other countries to strengthen their protection of intellectual property.

We are urging Congress to enact legislation, such as S. 573, that would prevent foreign manufacturers from obtaining free use of U.S. research and development by making pharmaceuticals abroad in violation of U.S. process patents and then exporting the products into this country. The legislation would strengthen the enforcement of process patents in the United States--and make U.S. law consistent with the laws of other industrialized countries.

Further, Congress should pass legislation--along the lines of H.R. 1115--that would help to rationalize a product-liability system that has become increasingly chaotic and unpredictable. Excessive judgments are being rendered against manufacturers. Huge windfalls are being awarded for "pain and suffering." And large sums are being inappropriately assessed against companies as "punitive" damages.

Congress also should pass legislation--such as S. 58--to restore the R&D tax credit and make it permanent. In addition, Congress should pass compromise legislation expected to be introduced soon that would provide for the automatic set-aside to U.S. income of 67% of the R&D costs of a U.S. multinational corporation that are incurred in this country. As it now stands, research and development costs for taxable years beginning after

August 1, 1987 will have to be fully allocated between U.S. and foreign income--a strong disincentive to expanding domestic R&D.

These steps would help to ensure that our industry--on the verge of what promises to be its most productive period--does in fact realize its full potential for improving public health. Our companies--in many cases using the exciting new techniques of biotechnology--are working to develop drugs to treat and cure such deadly diseases as cancer, heart disease, Alzheimer's disease and leukemia, among a host of other diseases.

Of most pressing importance, our industry is engaged in an all-out effort to conquer what is fast emerging as one of the most insidious diseases the world has ever known--AIDS. Of 11 products recently identified by The New York Times and Business Week as the most promising AIDS drugs, eight were discovered by private industry and all 11 are being developed by industry.

These new medicines will only come from the research-based pharmaceutical industry--and only if the industry's investments in research and development can be maintained.

Mr. Chairman, that concludes my full statement. I would be pleased to respond to any questions you or the other members of the Subcommittee may have.

Mr. **Waxman**. Thank you very much, Mr. Mossinghoff.

Mr. Watson.

STATEMENT OF DOUGLAS G. WATSON

Mr. **Watson**. Thank you, Mr. Chairman.

My name is Douglas Watson, and I'm the president of the Pharmaceuticals Division of Ciba-Geigy Corporation.

We at Ciba-Geigy and, I believe, all of us in the industry share your concern about the increasing cost of health care in this country. We recognize and accept that the pharmaceutical industry has to play its part in helping to minimize further escalation.

Mr. Mossinghoff showed earlier the prescription drug component of health care cost has declined from 14 percent to under 7 percent over the past 20 years. But what is even more remarkable is that the importance of the drug treatment component of health care has significantly increased over the same period.

Prescription drugs not only save lives and relieve suffering, but are becoming more and more essential as the most effective way to control the escalation in health care costs. Thanks to today's innovative prescription drugs, many people can lead more or less normal lives, able to earn a living, rather than being hospitalized as the result of a heart attack, epilepsy, or crippling arthritis.

I would therefore suggest to you that prescription drugs have in the past played and will in the future continue to play a very major role in controlling total health care costs.

We have come to expect longer, healthier, and more active lives, and we tend to take the contributions of modern prescription drugs for granted. But we must remember that today's innovative drugs are the result of R&D investments years ago, and unless we can afford to continue to make substantial investments in research today, we will not be able to develop innovative medical treatments for the future.

For our part, Ciba-Geigy invests worldwide more than $1 million per day on pharmaceuticals research and development, 17 percent of sales here in the U.S. Some 70 percent of that investment relates to innovative new chemical entities targeted at cardiovascular disease, Alzheimer's disease, AIDS, cancer, and disease-modifying antiarthritic drugs. Ciba-Geigy is firmly committed to the research and development of products that address these most difficult disease states, operating at the cutting edge of scientific knowledge. And to do so, Ciba-Geigy has increased its R&D budget by 98 percent over the last 5 years, far higher than its increases in prices at 52 percent.

But I know, Mr. Waxman, that you essentially accept all these aspects of our industry and that you want to address the specific question of our pricing practices. The factors affecting our pricing decisions are numerous and diverse. They include the high degree of risk inherent in the research, development, and use of our drugs; the extraordinary expense and time required to bring a new product to the market; the significant need for continuing capital investment to maintain state-of-the-art facilities to ensure regulatory compliance; the extensive funding of basic biomedical research outside the company; and the expenditures necessary for the education and informational activities for both medical professionals and patients; and, of course, the competitive environment we live in.

Individual product pricing reflects the value of the therapy provided and the competitive profile of the drug. But overall, our pricing must reflect a balance between our need to generate revenues to cover our operational costs, to fund our aggressive R&D programs, and, of course, to earn a reasonable profit.

The detailed pricing decision is a complex process. The competitive health care marketplace pits relatively low-cost prescription drugs against higher-cost alternatives such as surgery or extended hospital stays. And even within the prescription drug component of the health care market, pharmaceutical products compete in a therapeutic category against new classes of drugs, new chemical entities, established brand medications, and generics.

The cost of doing business has increased. Operational costs continue to grow as a result of increases in employee compensation, the need for a higher caliber of scientists and scientific equipment, and the need to hire more people to meet the ever more demanding regulatory requirements, and these include both FDA pharmaceutical requirements as well as Federal and State environmental requirements.

At the same time, the changing composition of the health care market has expanded the number and nature of the individuals participating in the drug selection process, and this has resulted in the need for incremental expenditures to reach the new and different players in the marketplace.

Innovation is the key success factor for our industry. Companies that do not successfully innovate will not survive. And as a result, companies invest heavily to bring new products with added value to the market, as well as continuously striving to add value to their established products with new indications and more convenient dosage forms.

In summary, therefore, pharmaceutical drugs are the most effective way to control total health care costs. Pricing in the pharmaceutical industry is complex and dynamic. It has to take into account many factors—the value of the therapy provided, the competitive profile of the product, the extraordinary expense and time required for research and development, the high degree of risk inherent in our industry, increasing regulatory requirements, the capital investment required, the cost of education and information for the physician, medical administrators, pharmacists and patients. Innovation is and will continue to be the key success factor for our industry and a corresponding benefit to society.

Balancing all of these considerations, Ciba-Geigy believes that our pricing practices have been reasonable and justified.

I thank you for your consideration.

[Mr. Watson's prepared statement follows:]

STATEMENT OF DOUGLAS G. WATSON

I. INTRODUCTION

The Pharmaceuticals Division of CIBA-GEIGY Corporation offers this testimony in response to a request from the Subcommittee on Health and the Environment regarding our price increases for prescription drugs during 1981-86. Factors affecting pricing decisions are numerous and diverse. They reflect a balance between our need to earn a reasonable profit in a highly competitive marketplace and our need to fund a sufficient amount of research and development to advance medical treatment.

Being a profit-making enterprise is entirely consistent with being a responsible corporate citizen. CIBA-GEIGY is certainly concerned about the impact of the prices we charge for medications, and we are proud of our record of accomplishment and service. The benefits and cost savings which our products have brought to millions of patients are profound.

In addressing the issue of price increases, several factors must be considered:

- The high degree of risk inherent in the research, development and use of new chemical entities (NCE's);
- The extraordinary expense and time required to bring new products to the market;
- The significant need for continuing capital investment to maintain state-of-the-art facilities and to ensure regulatory compliance;
- The extensive funding of basic biomedical research outside the company;
- The competitive environment, including both drug and non-drug alternative therapies; and
- The expenditures for education and information activities for both medical professionals and patients.

Balancing all of these considerations, CIBA-GEIGY believes that our price increases over time have been reasonable and justified.

II. PHARMACEUTICALS: A RISKY BUSINESS

The development of new drugs is a high-risk business. it requires the outlay of massive expenditures for research and development, with very uncertain prospects for return:

- Only one in approximately 10,000 new compounds synthesized is approved by the Food and Drug Administration (FDA);
- Only about 12 percent of the NCE's tested in humans are finally approved by the FDA;
- The average time required for a new drug to progress from synthesis through development to approval is now more than 10 years, roughly *double* the time required in the mid-1960's.
- Two out of every three drugs introduced in the U.S. market since 1970 by all pharmaceutical companies have not realized profits sufficient to recover research and development costs (Grabowski, 1982).

The estimated cost of research and development for each NCE requiring an approved New Drug Application (NDA) is over $100 million. In contrast, the average cost of preparing a generic product for market under an Abbreviated New Drug Application (ANDA) is estimated at $250,000.

Future Research Holds Even Higher Risks. Average expenditures of time and money continue to increase. As research expands into the "cutting edge" of science, such as the search for treatments for AIDS, Alzheimer's disease, cancer or for disease-modifying anti-rheumatics, costs rise significantly. Industry has greatly increased expenditures in order to expand the basic biomedical knowledge necessary to develop drugs for these more complex illnesses. In addition, because Federal funding has decreased in recent years, the U.S. pharmaceutical industry has increased its share of the funding of biomedical research and development. Indeed, it is projected that the pharmaceutical industry will fund more health research in 1987 than will the National Institutes of Health. The increased costs associated with basic research do not tell the whole story, however. The risks inherent in pharmaceutical research are related to the low probabilities of a synthesized compound being approved for sale in the U.S. market.

Unexpected Risks In Using A Drug. Risk does not end at the approval of a new drug, it just changes form. Drugs that look promising in the lab and in clinical trials sometimes have a rare, unexpected side effect that shows up only after a large number of patients have been on therapy. Adverse reactions may result in product liability suits. In view of the prohibitive costs of product liability insurance and the unrestrained costs associated with defending such suits, product liability concerns represent a serious risk for the pharmaceutical industry. In some cases, such as research on drugs for diseases affecting the reproductive system, the risks of doing research outweigh the benefits, and further research efforts have been terminated.

III. CIBA-GEIGY'S EXPERIENCE: COMMITMENT TO RESEARCH

CIBA-GEIGY is one of the leading companies in terms of research and development expenditures on pharmaceuticals. In the U.S. in 1986, 17 percent of CIBA-GEIGY's Pharmaceuticals Division's sales were devoted to research and development. This figure is higher than the national average of 15 percent for pharmaceutical research and development expenditures.

Our expenditures on pharmaceutical research and development in the U.S. increased by 98 percent between 1981 and 1986; prices increased during this same period by 52 percent. CIBA-GEIGY's research and development emphasis, moreover, has shifted dramatically toward NCE's. Dollars spent on NCE's rose by 172 percent between 1981 and 1986 and now account for nearly three-quarters of total research and development.

The continuing infusion of large capital expenditures also demonstrates the extent of our commitment to research and development. Since 1981, capital projects have exceeded $200 million. This includes four major new facilities, roughly half of our capital expenditures during this period, entirely devoted to increasing the productivity of our research and development efforts.

Risks To CIBA-GEIGY. CIBA-GEIGY, like all other companies in the industry, is vulnerable to the risks inherent in developing and marketing pharmaceutical products. CIBA-GEIGY's research and development costs are high; and the median time for development and FDA review of NCE's approved between 1977 and 1983 was 10.3 years.

Maintaining a revenue level sufficient to fuel research and development and to sustain a reasonable return is a primary business goal. However, at 98 percent, CIBA-GEIGY's 1981-1986 rate of increase in spending on research and development is far higher than its rate of increase in prices, at 52 percent. Moreover, even those drugs that have sustained the largest price increases remain among the lowest in price in their respective therapeutic categories.

IV. CIBA-GEIGY'S CONTRIBUTIONS TO HEALTH, RESEARCH, AND SOCIETY

A. *Improvements In Drug Therapy*

CIBA-GEIGY's research and development has produced significant advances in medical treatment, including new drugs, and new uses, new delivery systems and new dosage forms for existing drugs.

CIBA-GEIGY was the pioneer in the discovery of drugs for the treatment of cardiovascular disease. CIBA-GEIGY has also developed:

- the first advanced drug delivery potassium supplement in the world;
- the first drug for spasticity which acts at the exact site of the disease, used frequently for Vietnam veterans who suffered spinal cord injuries;
- the first anti-epileptic drug demonstrated to significantly reduce cognitive dysfunction in children with epilepsy;
- the first transdermally delivered medications in the world, which significantly reduce the amount of drug necessary to control such conditions as angina and menopause, improving the quality of life in thousands of patients;
- the first effective drug for thalassemia, which extends the life of those patients suffering from kidney disease; and
- the first human calcitonin, for the treatment of Paget's disease.

By improving patient compliance, our new delivery systems and dosage forms reduce health care costs. For example, our transdermal patches improve patient compliance and, by delivering medication at a more consistent rate, may help reduce adverse reactions.

Search For New Therapies. CIBA-GEIGY is seeking new treatments for diseases of particular concern to the public, such as AIDS, cancer and Alzheimer's disease. Three compounds show promise in the battle against AIDS. For cancer, our development plan calls for a 95 percent increase in spending on research during 1986-89. This substantial investment demonstrates our determination to be a leader in finding new therapies to fight this difficult group of diseases.

CIBA-GEIGY has recently received approval under the Orphan Drug Act to market Lamprene®, for the treatment of leprosy, and Cibacalcin®, for the treatment of a painful bone disease. The Orphan Drug Act has significantly facilitated the development of such drugs. However, full development costs are not likely to be recaptured. Before Lamprene's approval, CIBA-GEIGY regularly supplied a number of patients with this drug free of charge and continues to do so for some AIDS patients or investigational purposes. During 1985-86, more than a dozen other investigational drugs were also made available to patients without cost, in accordance with FDA's "compassionate" Investigational New Drug Exemption (IND) policy.

B. *CIBA-GEIGY: A Contributor to Health Care*

CIBA-GEIGY's contribution to better health care is not limited to our own research and development activities. In 1986 and 1987, approximately $7 million has been, or will be, given to universities and research foundations to fund basic biomedical research, not linked to studies in support of a particular NDA. Another $1 million has been or will be contributed to other medical institutions, professional organizations, disease-oriented consumer groups and other nonprofit institutions.

CIBA-GEIGY's innovative programs recognize the importance of the patient's participation in optimizing health care. In the past 2 years, we have conducted a series of dialogues with consumer interest groups to explore the public's views concerning such topics as improvements in drug therapy and the delivery of health services in a cost containment environment. The purpose of these sessions is to better understand the needs of the consumer and to help target our activities to meet those needs.

CIBA-GEIGY's $1 million contribution initiated the landmark National Council on Patient Information and Education (NCPIE). The purpose of this highly-respected organization is to provide consumers with the information they need and request about prescription drugs. Enhanced communication can help consumers take medicines more safely and effectively, help patients get better faster and avoid side-effects, reduce hospitalizations due to drug interactions, and increase patient satisfaction with professional care. Recently, NCPIE has established a special program to improve the flow of information to the older patient, who generally bears a greater risk of responding poorly to drug treatment.

V. PRICING IN A COMPETITIVE ENVIRONMENT

Prescription drug pricing is a complex process. The competitive health care marketplace pits relatively low-cost prescription drug products against higher-cost alternatives such as surgery and extended hospital stays. Even within the prescription drug component of the health care market, pharmaceutical products compete in a therapeutic category with new classes of drugs, new chemical entities, established brand medications and generics.

New products with added value entering the market at higher prices impact the unit volume sales of the established brands. Slower growth or decline in unit volume may result in price increases for established brands in order to continue to support the funding of critical research and development objectives. Continued development of established products through new indications and new dosage forms increases the value for the patient of established products compared to the competition. Increased value may result in increased price.

The changing composition of the health care market increases the complexity of pricing decisions requiring sufficient flexibility to meet the variations in the competitive environment. This changing composition also expands the number of customers participating in the drug selection process, thereby requiring incremental expenditures of funds to reach the new and different players in the marketplace.

Pricing of prescription pharmaceuticals must address all of the factors described above and result in sufficient revenues to fund continued investment in research and development and to maintain our position in an intensely competitive environment with a reasonable profit.

VI. DRUG THERAPY: A COST EFFECTIVE APPROACH TO HEALTH CARE

Prescription drugs account for a relatively small and decreasing proportion of the total health care dollar, totalling about 7 percent in 1986. Yet, prescription drugs are an excellent means of controlling health care costs. Their contribution to health care cost containment far exceeds the cost of prescription medications to the patient. Under the current system, we finance the treatment of diseases in their acute stages. Nevertheless, under numerous public and private insurance programs, we fail to provide the adequate coverage for those prescription medications capable of reducing the more expensive components of health care costs.

To control total health care costs, it would be wise to facilitate access to, and proper use of, prescription drugs. Careful drug prescribing by physicians and conscientious compliance by patients can minimize the number of physician visits and the cost of hospital care. Drugs can reduce the need for more expensive surgery and can help ensure the success of necessary surgery. For example, administration of a CIBA-GEIGY drug immediately following a heart attack significantly increases the prospects for successful recovery and reduces the possibility of a recurrent heart attack—and another expensive hospital stay.

In the decades to come, the "graying of America" will generate a greater need for cost-effective health care, resulting in increased utilization and institutionalization. Failure to adequately fund pharmaceutical research in order to develop safe and effective pharmaceutical therapies will continue to drive the elderly into the more expensive segments of the health care delivery system. If we are to control tomorrow's high health care costs, we must not attempt to limit revenues necessary to sustain today's research and development.

VII. CONCLUSION

We have come to expect a longer, healthier life. We often take the contributions of prescription drugs for granted, yet we have been reticent about accepting the trade-offs necessary to make these products available. Essential medications are costly. But the tremendous benefits and the cost-effectiveness associated with prescription drugs fully justifies the price.

Pricing in the pharmaceutical industry is complex and dynamic. Pricing decisions must address the highly competitive conditions within the overall health care market. The price of prescription medications funds our contributions to health care and supports the high cost of research and development. Monies invested decades ago yield today's innovative medical treatments for future decades. We do not believe that changes which would upset these dynamics are appropriate, particularly if the United States is to maintain its leadership role in bringing valuable and important medications to the public.

Thank you for your consideration.

Mr. WAXMAN. Thank you very much, Mr. Watson.

Let's hear from Mr. O'Neill.

STATEMENT OF DONALD E. O'NEILL

Mr. O'NEILL. My name is Don O'Neill. I'm executive vice president of Warner-Lambert Company. For your information, Warner-Lambert employs some 32,000 people and conducts business in more than 130 countries. We operate approximately 100 manufacturing plants and maintain research centers on 3 continents. Our prescription pharmaceutical business contributes approximately 30 percent of our $3.1 billion worldwide revenue. These sales are generated primarily by our Parke-Davis Unit, whose 120-year history is marked by significant medical contributions.

For example, Parke-Davis holds U.S. Biological License No. 1 and was one of the first pharmaceutical companies to be dedicated to medical research. As our response to your committee points out, over the past 3 years, price increases at Parke-Davis represent less than 6 percent of total revenue. That figure is significantly below the overall industry average.

In terms of 1986, our price increases, after all allowances and discounts, amounted to less than 5 percent. In contrast, our research investment was up 10 percent last year and will increase another 12 percent in 1987 to $227 million. On a dollar basis, our 1986 price increase volume and our research increase were approximately the same.

These numbers reflect Parke-Davis' substantially greater commitment to research and development activities. Since 1984, research and development investment has increased at a greater rate than sales. Over the next 5 years, an additional $1.3 billion will be invested. Looked at from another perspective, we are presently investing 16 percent of our pharmaceutical sales behind R&D programs. The overall industry average, as you know, is 15 percent.

Our research programs are managed on a worldwide basis out of Ann Arbor, MI, and we operate major research centers in the U.K, Germany, and Canada, as well as development laboratories in Japan, France, and Australia. In addition, over the past several years, we invested $100 million in new research laboratories in Michigan, New Jersey, and Germany.

But research isn't our only escalating cost factor. Take liability insurance, for example. In 1981, we paid a premium of $3 million for $200 million of coverage. This year our premium is $10.6 million; our coverage is $175 million, but to make that happen, we had to self-insure the first $25 million.

The aim of our research effort is to develop unique, patentable compounds which advance medical therapy and which provide a return to the corporation and its investors. We have concentrated on such disease states as atherosclerosis, cardiovascular disease in general, and cancer. We are pleased to report that several of these programs, including our 12-year coronary heart disease study in Finland, promised to help change medical practice.

But that's only part of the story. An important segment of our research effort is directed towards other life-threatening diseases affecting smaller portions of our population. Earlier this month, the lead article in the New England Journal of Medicine reported that an experimental drug had achieved a 96 percent response rate among leukemia patients. The drug was Pentostatin, synthesized in our laboratories in 1964, and over the past 20 years, we have evaluated the compound in a wide range of viral and cancer conditions. It always showed promise, but not at the level that regulatory or medical authorities would deem significant. Still we persisted. This month's report was highly gratifying.

Or take Trimetraxate. This is a compound whose activity against small-cell lung cancer looks very promising. In the course of our pharmacology, we discovered that its mechanism could provide advantages to patients with pneumocystis. As you may know, this is the infection that frequently claims the lives of AIDS victims.

This aspect of our AIDS research program is now underway, in concert with the National Cancer Institute.

Over the past 10 years, Parke-Davis has conducted leading edge research on learning disabilities. These range from children's dyslexia to Alzheimer's disease in adults. Based on that research record, we are now part of a team testing an experimental compound against Alzheimer's.

Research also continues on products that are already on the market, even those off-patent. Meclomen is a good example. This is an nsaid developed by Parke-Davis in 1967. According to an FDA report, it combines effectiveness with one of the best side effect profiles.

After getting meclomen on the market, however, we didn't stop our research and regulatory effort behind it. We now have three supplemental claims before the FDA involving analgesia and various menstrual discomforts. And we also have programs at Ann Arbor aimed at producing injectable, sustained and immediate release product forms.

Meclomen is not a big product—less than $30 million this year—and it does have significant generic competition. Its patent expired three years ago, but since new dosage forms provide an opportunity for better patient compliance and ease of administration, we'll keep at it.

Our ability to develop new dosage forms was part of our rationale in creating our new generic division last year. The Waxman-Hatch Bill of 1984 has significantly altered the marketplace. Last year, some 600 ANDA's were approved by the FDA. In contrast, approvals for NCE's, new chemical entities, amounted to 20.

The opportunities for Warner-Lambert are obvious. We have 120 years of pharmaceutical know-how, manufacturing expertise, and marketing experience. We have the ability to transform older compounds into more elegant dosage forms, including injectable sustained-release and IV formulations.

As a 37-year participant in the pharmaceutical business, I'm proud of our industry's achievements. Newsweek has called our products "enchanted substances," which give physicians their first true power to cure. The extension of life since 1950--more importantly, its improved quality—is a direct function of our research, research that provides value that cannot readily be measured.

In that sense, I don't believe it is statistically fair to focus on a 3- to 5-year period of pricing history, nor do I believe it is fair to focus on the price of a single product without reviewing an entire line of hundreds of individual items. If we are going to compare drug prices with the CPI, let's look at the record since the index was created, and let's also look at the validity of using an index that is heavily influenced by energy and transportation costs.

If you subtract these two elements, I am told that the CPI rose 4.7 percent last year, and that was precisely Parke-Davis's increase last year. I would also like to point out that the CPI does not measure advances in products or technology.

However, I'll leave these discussions to the economists and the more learned among us. I suspect they could validate the billions of dollars generated by lives saved, surgeries avoided, and hospitalizations shortened by the intervention of those "enchanted substances."

The fact is that the fruits of pharmaceutical industry research, operating in a free market, have contributed importantly to everyone in this room today, and with your help, Mr. Chairman, and your committee, we'll continue to serve.

Mr. WAXMAN. Thank you, Mr. O'Neill.

Mr. Clark.

STATEMENT OF PAUL N. CLARK

Mr. CLARK. Good morning. My name is Paul Clark, president of the Pharmaceutical Products Division of Abbott Laboratories.

Mr. Chairman, on February 20, you asked a number of specific questions about Abbott's sales revenues, marketing and R&D expenditures. As you know, we have submitted confidential responses to those inquiries, so we will not attempt to comment directly on those today. However, to give you and the committee a perspective on Abbott Laboratories and the markets we serve, I would like to make some general comments.

Abbott is proud to be able to provide patients with a broad line of high quality, cost effective prescription drugs. U.S. prices for Abbott's prescription drugs on average have declined over the past 2 years and since 1981, the average price increases for U.S. prescription drugs increased only 1 percent per year.

I want to point out, however, that Abbott is much more than a prescription drug company. Abbott Laboratories is unique in that it has one of the most diverse lines of health care products in the industry. This includes diagnostics, hospital products, medical nutritionals as well as prescription drugs. In fact, over three quarters of our annual sales come from health care products other than prescription drugs.

To remain competitive in these multiple markets, we must continually generate new technologies that not only improve the quality of patient care but are cost effective to health care providers as well. This means we must make a substantial commitment to research and development directed at high quality, cost effective products in a variety of health care categories.

Abbott's total R&D expenditures have increased significantly in recent years. Last year, Abbott spent $285 million in research and development, an increase of 18 percent over 1985. During the last 5 years, our R&D investment has grown at an average annual rate of 20 percent, much higher than our comparable increase in sales.

A large portion of Abbott's total R&D expenditure went to developing new diagnostic tests for hepatitis, cancer and AIDS and other important disease conditions. This effort has achieved results. For example, Abbott was the first company to market a test for antibodies for the AIDS virus. We are now marketing more sensitive and selective antibody tests in the U.S. and Europe.

This year we expect to seek FDA approval for a test that detects antigens to the AIDS virus. The antigen test is important because it detects the presence of the AIDS virus in the blood much earlier than the antibody test and also provides a clear indication of who is likely to actually contract AIDS.

Abbott has also made a substantial commitment to R&D aimed at prescription drugs. Our prescription drug R&D expenditures have increased 128 percent since 1981, a significantly higher rate than our sales growth. These R&D figures do not include research done with other companies, joint ventures, nor do they include other expenses that are normally associated with intensive research efforts.

About 80 percent of Abbott's prescription drug R&D expenditures can be attributed to new chemical entities. This does not include what we spend on improvements in dosage forms that lead to better patient compliance and research on already approved products for new treatments.

A recent result from our prescription R&D efforts includes Hytrin, the first once-a-day prescription drug in the antihypertensive alpha-blocker category, that we expect will receive FDA approval this year after 12 years of costly R&D efforts.

Also pending approval is TRH, an orphan drug for the symptomatic relief of Lou Gehrig's Disease. We are already marketing another orphan drug, Panhematin, for the control of a hereditary blood disorder that attacks only about 5,000 women annually. Later this year we expect to file a new drug application for Surfactant TA, the first drug to treat hyaline membrane disease, a respiratory disorder that is the leading cause of death among premature babies. Each of these products, by the way, is a new chemical entity.

In summary, Abbott Laboratories is a broad based health care company that invests heavily in research and development. This effort has produced a diverse and continuous flow of new health care technologies ranging from prescription drugs that treat cardiovascular disease and medical nutritionals that speed patient recovery to devices that monitor critically ill patients and diagnostics that detect antibodies to the AIDS virus.

Abbott has invested substantial funds for the discovery and development of new and better prescription drugs. At the same time, Abbott's prices on average in the U.S. have increased 1 percent per year over the last 5 years, far less than the rate of inflation.

This completes my testimony.

Mr. WAXMAN. Thank you very much, Mr. Clark. Mr. Shoff.

STATEMENT OF HARRY SHOFF

Mr. SHOFF. Mr. Chairman, members of the subcommittee, I'm Harry Shoff, president of Winthrop Pharmaceuticals, the ethical pharmaceutical division of Sterling Drug. I will summarize my statement.

I welcome this opportunity to point out that more than 54 percent of Winthrop's sales are in the hospital segment of the market. In fact, our largest selling product, Omnipaque, a contrast media agent used in hospital radiology, is not a pharmaceutical product and is not sold in drug stores.

Winthrop is a research oriented company dedicated to health care innovation. Pharmaceutical research is both risky and expensive. In 1970 it was estimated that it took 5 to 7 years and cost $3 to $5 million to develop a single marketed product. PMA's figures suggest that today it will take approximately 7 to 10 years and cost well over $100 million to develop a marketed product. It also should be noted that in terms of a company's economics, there are many more failures than successes.

As a percentage of total prescription sales, our research and development expenditures exceed the industry average and have produced such products as Inocor for acute congestive heart failure and Modrastane for the treatment of Cushing's disease. Modrastane is a very small market for sure. However, to the 5,000 sufferers of Cushing's, it is very important.

Nearly all of Winthrop's prescription products compete in small markets. They are niche products for acute care which address the important medical needs of a small part of the population.

Winthrop's contribution to the future of pharmaceuticals is exciting. Allow me to highlight just a few of our current research projects.

We recently submitted an NDA for Corotrope, a new cardiovascular agent with vasodilating and inotropic properties for the treatment of a broader segment of the population with congestive heart failure. We continue to develop new and unique analgesic agents that will control pain without gastrointestinal side effects and physical dependence.

Most of our current product line are off patent. One such product, Danocrine, is used in the treatment of endometriosis, a painful disorder that can lead to infertility. We treat annually 30,000 women of child bearing age. Surgery is the alternative therapy, a much more costly option.

We also have funded a major university to develop a non-invasive diagnostic test for endometriosis which is currently diagnosed by laparoscopy at a cost of $1,500. Our new diagnostic test unit should be a fraction of this cost.

Mr. Chairman, the daily cost therapy of almost all of our products is substantially less than competing therapies. Further, for the period 1981 to 1986, Winthrop increased prices for all products an average of 8.8 percent. Our research and development expenditures were up 9.2 percent. In fact, Winthrop's R&D expenditures as a percentage of total U.S. prescription sales greatly exceed the industry average.

As Mr. Mossinghoff has pointed out, exploding costs of insurance coverage has affected the price of pharmaceuticals. The availability of Winthrop's insurance coverage decreased substantially for events occurring after July 1985. We are essentially self insured for liability coverage. Millions of dollars of reserve funds have been set aside for such protection. Capital costs are another factor.

We have underway a multi-million dollar capital improvement program to modernize our research facilities for drug discoveries. Winthrop is committed to the discovery and development of new and superior compounds in areas of important medical needs.

Our products have an important place in their competitive markets and our decisions reflect our business environment.

Mr. Chairman, thank you for the opportunity to express my views to the Subcommittee.

[The prepared statement of Mr. Harry Shoff follows:]

STATEMENT OF HARRY SHOFF

Mr. Chairman and members of the subcommittee, my name is Harry Shoff. I am President of Winthrop Pharmaceuticals, the prescription drug division of Sterling Drug, Inc. My testimony today is in response to your letter of March 23 requesting that we appear and address the subject of recent prescription price increases.

Our business is currently focused on cardiology, radiology, obstetrics/gynecologic medicine, and nalgesics. Our largest selling product, Omnipaque, a contrast media agent used in hospital radiology procedures to produce better visualization in X-rays, is not a pharmaceutical product and is not sold in drugstores. In fact, more than 54 percent of Winthrop sales are in the hospital segment of the market where diagnosis related groups and pharmacy and therapeutics committees act as effective cost control measures.

Winthrop is a research-oriented company dedicated to health care innovation. Pharmaceutical research is both risky and expensive. In 1970 it was estimated that it took 5-7 years and cost $3-$5 million to develop a single marketed product. PMA's figures suggest that today it takes approximately 7-10 years and costs well over $100 million to develop a marketed product. It also should be noted that, in terms of a company's economics, the successful drug must carry the cost of failures, that is, the compounds for which testing was initiated but abandoned.

As a percentage of total prescription sales, our research and development expenditures exceed the industry average and have produced such products as Inocor for acute congestive heart failure and Modrastane for the treatment of Cushing's disease.

Modrastane (trilostane) is currently marketed by Winthrop for the treatment of Cushing's disease, an illness of hyperfunction of the adrenal glands. Modrastane is not a well known drug. However, to the 5,000 sufferers of Cushing's, a particularly debilitating disease characterized by obesity and muscular weakness associated with adrenal or pituitary dysfunction, it is very important. A very small market for sure, but a compound with potential for other indications.

We are conducting clinical studies with Modrastane in the management of metastatic breast cancer in post-menopausal women.

Winthrop's contribution to the future of pharmaceuticals is exciting, if you will allow me to highlight just a few of our current research projects.

We recently submitted an NDA for Corotrope (milrinone), a new cardiovascular agent with vasodilating/inotropic properties for the treatment of a broader segment of the population with congestive heart failure. Clinical studies with Corotrope indicate a significant improvement in exercise tolerance for the cardiac patient without increased perceived exertion. We may take for granted something as common as walking up a flight of stairs but for the cardiac patient, that can be a challenge.

We continue our effort to develop new and unique analgesic agents. WIN 48908-6 is one of these compounds that will control pain of mild-to-moderately severe intensity, without gastrointestinal side effects and without the expectation of physical dependence. Studies have been conducted which suggest that this compound may selectively inhibit brain prostaglandin synthesis.

One characteristic of nearly all of Winthrop's currently marketed prescription products is that they compete in small markets. They are "niche" products which address the important medical needs of a small part of the population, and generally are not indicated for chronic illnesses. Winthrop's products are used for acute care.

Most of our products are off-patent. For example, Danocrine, an off-patent product product, is used in the treatment of endometriosis, a little known but painful disorder that can lead to infertility. The patient population that we treat annually is about 30,000 women of childbearing age. The alternative therapy available to infertile women is invasive laser surgery, a much more costly option requiring hospitalization and attendant lost wages, etc.

Winthrop made a major commitment with the American Endometriosis Association to disseminate appropriate information about this disease category to young women. This commitment took the form of an educational campaign in national women's magazines to highlight the linkage between infertility and endometriosis.

We also have funded a major university to develop a non-invasive diagnostic test for endometriosis which should dramatically increase correct diagnosis of the disease. Currently, endometriosis is diagnosed by laparoscopy at a cost of approximately $1500 a procedure. Our new diagnostic test unit should be a fraction of this cost and will facilitate routine screening by primary care physicians. In addition, we are working on sustained-release dosage forms for Danocrine which should reduce costs while providing equal efficacy with fewer side effects.

Significantly, the daily cost of therapy of almost all of our products is substantially less than competing therapies. For the period 1981-1986, Winthrop increased prices for all products an average of 8.8 percent. By contrast, Winthrop's research and development expenditures during the same period were up 9.2 percent. As you know, Winthrop's research and development expenditures as a percentage of total U.S. prescription sales greatly exceed the industry overage.

The escalating cost of research has been documented as a major factor which determines price increases, but there also are other elements to consider.

As Mr. Mossinghoff has pointed out in his statement for the PMA, the spiraling increase in the cost of insurance coverage is another example of a very real factor affecting the price of marketed products, including pharmaceuticals. In recent years, there has been a continuing general decline in the availability of appropriate product liability insurance coverage. As a result, Winthrop's insurance coverage decreased substantially for events occurring after July 1985. Thus, Winthrop is essentially self-insured for liability coverage. We had to set aside millions of dollars in reserve funds for such protection.

Capital costs are another factor. We have underway a multi-million dollar capital improvement program to modernize our research facilities for new drug discovery.

We remain committed to the discovery and development of new and therapeutically superior compounds to be marketed in areas of important medical need.

Winthrop drugs do have an important place in the markets in which they compete and our pricing reflects the business environment in which we operate.

Mr. Chairman, thank you for the opportunity to express our views to the subcommittee.

Mr. **Waxman**. Thank you, Mr. Shoff.

Mr. Mossinghoff, let me start with you. I want to agree with you that modern medicines have made a very important contribution to our Nation's health and we are holding this hearing precisely because drugs are essential to millions of Americans, but the medical importance of drugs does not explain to me why companies have raised their prices at unprecedented rates.

At our July 1985 hearing and since, you and your member companies have insisted that you have had to raise prices in order to spend more on research and development. Of course, that holds the promise for new breakthroughs and we all want to support increased research and development.

As you know, our subcommittee conducted a survey to evaluate this claim. We compared the increases in R&D expenditures with the increases in revenues due to price increases and quite frankly, your industry's own data don't support your claim. As you also know, we surveyed 24 of your largest companies which account for roughly ⅔ of the industry sales.

We found that in 1986, they raised R&D by $400 million but we further found that they generated over $1 billion from raising prices, several times what they needed to cover R&D increases. Moreover, between 1982 and 1986, while R&D expenditures rose by $1.6 billion, revenue from price increases jumped $4.7 billion.

It's clear to me that based on what your members have furnished to us that their prices are far in excess of what they need to fund the increases in research and development.

In view of these figures, how can you insist that research and development explains the industry's enormous price increases?

Mr. MOSSINGHOFF. First, Mr. Chairman, let me say that I know I've never said that all of the money resulting from price increases went into research and development. Research and development expenditures is one of the key areas where our companies are investing more and more, as my charts have indicated. I have not had a chance to look at your staff's report. For example, I don't know whether the $4.7 billion is before or after taxes.

Do you know the answer to that? That would make a big difference. If it is just revenues from sales, obviously the companies have to pay taxes on those revenues. We are a very high taxed industry among other industries.

Mr. WAXMAN. On the other hand, we could calculate that we give R&D tax credits for the research investments that the companies make. At any point, what you are saying to me is that you agree with the fact that the increases in prices were in excess of the R&D costs and your point is R&D costs are only one of the factors?

Mr. MOSSINGHOFF. But it's a very important factor in the increases in prices, I imagine. Let me say at the outset, Mr. Chairman, that one of the things that a trade association must stay far away from is pricing policies of our members. We don't discuss prices at PMA. PMA plays no role in the setting of prices.

To fund the enormous increase in research and development, that is a key factor in the increase in prices. It obviously pays taxes. It pays for all the other increases including product liability and the rest.

Mr. WAXMAN. They have to pay taxes. They have to pay for product liability insurance. They have to pay for all the work done by their employees. They are also paying for an increase in promotional costs that is equivalent to the increases that are now going into R&D. In fact, you and your members have insisted that recent jumps in prices should be attributed primarily to the need to expand R&D but if you look at the figures that have gone into increases over the last 5 years, from 1982 to 1986, your members spent $12.9 billion on marketing and detailing, while spending $12.5 billion on R&D. In effect, they have spent more on marketing and detailing then on R&D.

It seems to me that that ought to be very much on the table, and we ought to recognize that when consumers are being asked to pay these ever increasing enormously high prices far in excess of the increases in any other product or service in this country, that they are paying certainly for R&D increases, but that's only a small part of it. They are also paying an equivalent amount and in some cases even more for the marketing and detailing of these drugs. I want to go into why that is the case.

Let me ask a question of Mr. Watson. Mr. Watson, you and several other witnesses compared statistics in a way that I find extremely misleading. At two points in your testimony you stressed that Ciba-Geigy's 1981 to 1986 rate of increase in spending on research and development was higher than its 52 percent increase in prices, but any comparison of these percentages without knowing the actual amounts to which the percentages apply is meaningless. That is, without knowing the actual dollars involved, someone reading your testimony might conclude that you actually spent more money to increase R&D than you received from price increases.

In fact, the opposite is true. Isn't it correct that your company received many more times the amount of money from price increases than it spent to increase R&D during the period of time you cite?

Mr. **Watson**. The simple answer to your question, Mr. Waxman, is yes. It was certainly not my intention to infer to you that I was increasing R&D more, putting more dollars in than coming from price increases. The statistics nevertheless were correct, you look at the amount of money we invest in 1986 versus 1981, we have doubled our investment in R&D.

Mr. **Waxman**. It seems to me to be misleading when you imply that a higher percentage of a smaller amount comes to more than a smaller increase of a larger amount. That's why we get this misleading notion that R&D is the reason why all these price increases have taken place, when you talk about higher percentage increase in R&D and a lower percentage in the price of the drug.

In fact, the increase for the cost of the drug more than pays for the increase in the R&D.

Mr. **Watson**. If you would permit, could I address your question? I think you are asking a very simple question which is not an easy one to answer, how do we calculate the price increases. You have to recognize that our total——

Mr. **Waxman**. I was asking you specifically whether you in fact had a higher revenue produced as a result of your increases in prices as opposed to the amount of dollars you spent on research and development.

Mr. **Watson**. Yes.

Mr. Waxman. Mr. Whittaker.

Mr. Whittaker. Thank you, Mr. Chairman.

I would like to direct my first questions to Mr. Shoff. You mentioned, Mr. Shoff, in your testimony, that most of the products you are manufacturing are off patent. Could you compare the pricing structure of your products with competing products?

Mr. Shoff. Quite large on average after our price adjustments over the last 2 years. Our prices are still relatively competitive with the leaders in the marketplace. As an example, we have a product called Placquinil that is used in rheumatoid arthritis. Placquinil on a treatment day cost is $0.70 to the patient. I found out just the other day that the least expensive ride I can take on the D.C. Metro is $0.80, on a comparative basis.

Like Placquinil, most of our products are used in acute care or severely ill patients and as such, they are very highly sophisticated and focused on a very small segment of the market.

Mr. Whittaker. Would you comment on your reference on page 4 of your testimony? You mentioned the niche products. Could you expand on that?

Mr. Shoff. A niche product is a small segment of the population, a small number of patients. Here again, let me give you an example. Inocor, which is a product that is used in hospitals, it's intravenously used, it is a product used for congestive heart failure, the end stages. Actually what it does, it gives and modifies the weaning heart to provide it with a few more days or weeks in order for surgery to be performed. Inocor again competes in a very small niche market, few patients, very, very highly sophisticated type of drug.

Mr. Whittaker. Thank you. I am going to direct my next question to Mr. Mossinghoff.

What are the problems and your awareness with the Canadian licensing system for pharmaceuticals?

Mr. Mossinghoff. Well, the Canadians have a system now that was enacted in 1969 in which in effect they take away all the exclusivity that goes with the patent and require compulsory licensing for virtually a nominal amount. It's a 4 percent rate of royalty. As soon as the compulsory license is issued, someone who doesn't bear the expense of the research and development, doesn't bear the expense of marketing, it's an educational effort with the physicians, the people that do not bear that expense are competing with them and pay only 4 percent to the pioneer.

The Canadians are attempting to change that now. I think they see their system is not serving them well. It's the only such system in the world of compulsory licensing for pharmaceuticals and they are changing it now to provide some exclusivity, 7 years or 10 years, depending on the circumstances, exclusivity to the pioneer inventor.

We view that change as significant. They are moving in the right direction. On the other hand, even with that change, they will still fall far short of the protection given pharmaceutical patents in all of the developed countries of the world.

Mr. Whittaker. The practical effect of that legislation that exists on the Canadian side then is what?

Mr. Mossinghoff. The practical effect is it would not in any way support or be an incentive to research and development. I believe if other countries with bigger markets were to adopt that, you would see those charts where the research and development expenditures are going up. You would see those R&D expenditures turn sharply down.

Mr. **Whittaker**. Beyond just theory, that is experience. That is what Canadians are experiencing in practice?

Mr. **Mossinghoff**. That's right.

Mr. **Whittaker**. What do you see in the nature of the people who sue pharmaceutical companies? Are they generally people who have not received the drug or should not have received the drug in the first place or are they people who simply had an idiosyncratic reaction to the drug?

Mr. **Mossinghoff**. I would say there are a number of cases of the latter where all drugs, if they are going to be effective, will produce side effects in some small percentage of the population. The physician who prescribes the drug does in effect a risk/benefit analysis each time he prescribes a drug. I totally disagree with Mr. Gordon, the witness before. I think physicians do an extremely wonderful job in selecting just the right drug for the right patient and need a wide diversity.

In any event, there are situations where the liability was found, enormous liability was found in cases where, for example, something happened, a kidney problem occurred. There's one case where a kidney problem occurred. The company didn't warn against it but it informed the Food and Drug Administration right along of all the situations involved in the clinical tests and the Food and Drug Administration felt that the kidney warning was inappropriate. That was the basis, the lack of the warning that the drug manufacturer did not include on the labeling because the Food and Drug Administration found it to be inappropriate. That was the basis for liability in that case.

We can give you any number of cases for the record to respond to your question, if you wish.

Mr. **Whittaker**. Thank you, Mr. Mossinghoff. Mr. Chairman, thank you for the time. I would comment that I believe this is another example of why this Congress needs to address the product liability problem. It is impacting on pharmaceutical companies. We have had testimony in this committee, particularly in the area of orphan drugs, in that our current court system is actually inhibiting products being available to consumers and the costs in some cases for litigation and insurance are outrageous.

Thank you.

Mr. **Waxman**. Thank you, Mr. Whittaker. Mr. Wyden.

Mr. **Wyden**. Thank you very much.

Mr. Mossinghoff, if I might, we have worked together on a lot of legislation, drug diversion and a variety of other things. I want to work with you on this. To do that, we are going to have to take on some gut issues with respect to pricing.

The first issue I want to start with is the generic drug issue. You heard one of the earlier witnesses from the senior citizens' group who said the rate of the price increase for the generic drug is nowhere near as high as the rate of price increases for A brand named drug.

It's my understanding that at the last hearing on drug pricing, held by Chairman Waxman, you said that because you had been at the PMA fairly recently, that you couldn't take a position on whether the American public could be assured that generic drugs were as safe and effective as the brand name drugs.

Given the fact that you have had a longer tenure here, could you now take a position on this issue. Could you give the American consumer the assurance that these generic drugs, which are going up in price at a less rapid rate than the brand names, are as effective and capable as a brand name?

Mr. MOSSINGHOFF. Congressman, we worked very hard at PMA to produce what we think is a totally documented, totally responsible statement to the Food and Drug Administration when they held their hearing, which I believe was back in October, September 29 to October 1, 1986. This was the PMA submission. We would be pleased to make that available to the committee.

It is our position that generic drugs can and really must be as safe and effective as the pioneer drug. The Food and Drug Administration——

Mr. WYDEN. But my question was: Are they? I want to know if PMA is going to give the consumer the assurance that they are as safe and effective.

Mr. MOSSINGHOFF. We have trouble with the Food and Drug Administration's tests for generic drugs in some therapy classes. In many therapies there is a broad range of when the drug can be made effective. The Food and Drug Administration generally uses what is called a 20/20 test, and that is that in a given number, a couple dozen of healthy males, the plasma concentration of the drug must be within plus or minus 20 percent of the plasma concentration for the pioneer drug.

In some cases, that test, we think is not as sharply defined. It led, for example, in November to the Epilepsy Institute putting out a physician's alert saying that some anti-convulsant drugs were not effective, and it was not so much the switch from a brand name to a generic. What the Epilepsy Institute's alert had to do with was switching among generics or from a generic to a brand name.

So I am not in a position, Congressman, to give you that assurance, and we are urging Dr. Young and Mr. Norris to address some of the issues that we raise in our submission to the Food and Drug Administration.

Mr. WYDEN. I would hope we could get a clear position from the PMA on the generic drugs since there is no documented evidence of therapeutic problems with the generics, and we are going to hear from Mr. Norris later.

One last question, which deals with the AZT and the fact that it costs $10,000 for a year's dose. I asked some questions of the Burroughs Welcome Company when they were here before, and I walked away with the conclusion that they were setting the price at random. When we tried to get into the specific questions of recovery of R&D, my understanding was their R&D costs were something like $80 million and they were going to make $1 billion in the first year. They really didn't seem to have any calculations on how much Medicaid might pay.

The only conclusion I drew was they were not going to explain how they arrived at these figures. Here we have a situation where a huge number of Americans are desperate. You are familiar with the suffering, I am, everyone is. What do you think of this situation regarding something that is so desperately needed, and the principal company in the field won't explain how it arrived at the figures? Do you think that is acceptable in the pricing area?

Mr. **Mossinghoff**. Congressman, I walk a long way around the pricing decisions of our companies and their marketing and explanations of pricing. PMA just doesn't get into that, nor can we get into that.

Mr. **Wyden**. But you think there is nothing wrong and that this is proprietary and they ought to be able to decide what they are going to charge. Yet when legislators ask them how they arrived at the figure, they shouldn't have to explain and they can just set any price they want?

Mr. **Mossinghoff**. I really would have to defer to their judgment of what is proper, Congressman.

Mr. **Wyden**. The only other question that I wanted to ask is why it seems the drug pricing situation doesn't lend itself to a competitive market? It appears that in the past, competition among drugs that were similar drove prices down; now it seems to drive prices up. I am in favor of a free market for prescription drugs, but certainly when I hear evidence like that, it doesn't seem the free market works very well.

Mr. **Mossinghoff**. Congressman, as I point out in both my summary and my prepared statement, there is really a shrinking window of time during which the pioneer drug companies can recoup their research and development, their marketing expense, their educational expense, and that period is being narrowed, one, by the fact that the generic competition comes on exactly the day the patent expires, on the one side, and on the other side, despite the fine efforts of Commissioner Frank Young and John Norris to cut back on the time that it takes to approve a drug, the facts are that those times are increasing. It is almost up to 3 years for new chemical entities.

So there is a narrowing period of time during which the recoupment of R&D and other expenses can be had. At the time of the patent term restoration legislation, there was a prediction by a scholar of the field that the patent term restoration ANDA legislation would produce two kinds of drugs, those that are off patent and cheaper, and those that are on patent, and because of the competition, the prices go up to recoup the investment made in those drugs, which is well over $100 million.

Mr. **Waxman**. Thank you, Mr. Wyden.

Mr. Bliley.

Mr. **Bliley**. Thank you, Mr. Chairman.

Mr. Chairman, this report that I heard you mention earlier, have you got a copy of it that we could have? I haven't seen it, and the counsel tells me we haven't had one available.

Mr. **Waxman**. It is in your folder, Mr. Bliley.

Mr. **Bliley**. Thank you. Thank you very much.

Mr. Watson, some allegations have been made by consumer groups earlier this morning that research and development is a thin disguise for advertising and marketing expenditures. Could you discuss in greater detail what components of your expenditures fall under the category of research and development?

Mr. Watson. Gladly. In our response to the committee, in the confidential response we classified R&D as all the expenses associated with the initial discovery, the biology, the chemistry, investigations of new approaches, innovative approaches to disease entities, mechanistic approaches we use, coming right through our process of putting it into animals to test the safety and toxicology of the drugs, and then ultimately when that is proven safe, into man for the phase one, phase two and phase three trials, and the submission of the NDA down at the FDA and getting approval.

The total expenses associated with that activity is what we have described as R&D. I think the inference was that market research and such type activities were also included. Those were not included in our response.

Mr. Bliley. Thank you, Mr. Watson.

The Congress has affected the prescription drug business in the last few years with legislation like patent term restoration, the ANDA bill and the diversion bill this committee recently reported. Would you give us your comments on what effect these laws might have on drug prices?

Mr. Watson. I think the individual bills have a timing difference impact on the industry. If one takes the drug competition bill or the Waxman-Hatch Act of 1984, I think that is a two-act play, if you will. In the first act there was a significant benefit to the generic companies who came in and found or were given an easier process to get an ANDA approval for generic drugs, and the benefit to the branded side of the industry was a longer patent protection, longer protection of our innovation when we come to the market.

The second act is still to come. I believe the act is working. I believe we are seeing the impact on our industry, but we have to wait a few years yet till we see the benefits of longer protection of our drugs when we bring them out under the auspices of this act.

In terms of the drug diversion aspects of Mr. Dingell's concerns, we support his concern. We can support Congress' concern for the need to eliminate drug diversion. That is absolutely not in our interest as an industry. Once again, it is an additional cost element which is part of our costing structure within our business.

So regulation and environmental regulation are increasing the costs that we have to bear within our industry.

Mr. Bliley. Thank you.

Mr. Mossinghoff, your fourth chart shows R&D expenditures as a percent of drug sales increasing from approximately 12 percent in 1980 to their current level of about 15 percent. How do you account for that?

Mr. Mossinghoff. Congressman, when I first came to this job a little over 2 years ago, I made it a point to get around and meet the people in the industry. I think it was probably on a plane from New Jersey late at night when the thought struck me that the response to all of the pressures that I have indicated—generic competition, the drug approval times at the Food and Drug Administration, regulation, international patent powers—the response of the industry so far has been more and better research and development. That is just about a uniform response among the PMA members.

I think it was alluded to today that only the very innovative companies are going to survive in this new environment that we find ourselves, so at this point I think the competition is driving each of the companies to increasing their research and development expenditure. The net result, obviously, is a pay-off to the people of the United States and the people of the world who are going to benefit from those expenditures.

Mr. **Bliley**. Thank you.

On Chart 5 you compare something you call an R&D index with the consumer drug price index. What is the R&D index, and how did you arrive at it?

Mr. **Mossinghoff**. The consumer price index was invented by economists in 1967. They said you are going to take a basketful of something and you are going to identify that and define that as a 100, and then from there on, if prices go up or down in that mix of products, you are going to track the index. Of course, for pharmaceuticals, the price index now stands at 288. For everything in the consumer price index, the index stands at 331.

We did that same thing with the research and development. We said that we will start with the R&D that the industry does in 1967, define that as 100, and we will track in the same way the index, and we end up at 1008, which is, as I indicated, 3.5 times what the prices in drug increases have been.

Mr. **Bliley**. Thank you.

Thank you, Mr. Chairman.

Mr. **Waxman**. Thank you, Mr. Bliley.

Mr. Coats.

Mr. **Coats**. Thank you, Mr. Chairman.

Mr. Shoff, I think you gave me some of the figures I was looking for, and one of them was just confirmed by Mr. Mossinghoff. That is that the average industry expenditure on R&D is running 15 percent. Is that correct?

Mr. **Shoff**. Yes.

Mr. **Coats**. You also mentioned that the average cost to bring a drug to market was $100 million. Mr. Mossinghoff, does that square with the industry-wide figures? That was maybe your average cost.

Mr. **Shoff**. Yes, sir, that is what I was using.

Mr. **Mossinghoff**. Yes, Mr. Coats. We arrive at a number of about $113 million now. The way we arrived at that is we did a detailed study in 1976 and updated that study using the government's biomedical research and development deflater. We do have a study that is just about complete now to update that number, but well over $100 million is a number that we can all stand behind as the average.

Mr. **Coats**. Do you all stand behind the figure of an average time to bring a drug to market of 7 to 10 years?

Mr. **Mossinghoff**. That is the industry average.

Mr. **Coats**. Earlier when we were talking about marketing, I believe you wanted to respond to one of the questions raised about the amount of expenditures in marketing a drug versus the amount of money going into R&D, and I was curious about what your answer would be.

Mr. MOSSINGHOFF. Mr. Coats, the point I was going to make was that sometimes promotion and advertising is used pejoratively, but in our industry, with the very skilled sales representatives, that is really an educational effort which is quite successful and has proven successful in educating doctors about the newest in therapy, educating them about the contraindications, the warnings to make sure that the doctors in their day-to-day practice are aware of new drug therapy.

Because the window during which the research base companies can recover their research and development and other expenditures is a narrow one, it is very important to them from an economic point of view to educate doctors very quickly on the new drug therapies. It also is an effort which has immediate payout to the people of the United States because it is through that that doctors become familiar with the new drugs and are able to treat their patients with new drugs and they are aware of, as I say, not only indications and benefits but also they are aware of the warnings and contraindications.

Mr. COATS. So we are not talking about a 30-second Miller Lite beer commercial type of marketing. We are not going to turn the TV on and see one drug company trying to gain market share by promoting the virtues of its new drug. When you talk about marketing and detailing, we are not talking about TV advertising or radio advertising—I am talking about prescription drugs now—billboards, the typical type of marketing practice that comes to most peoples' minds.

Mr. MOSSINGHOFF. We do not market to consumers. We market only to health care professionals, to the doctors. That is the marketing that we do, and it is detail men, it's brochures, it is education for these very able doctors that use our medications.

Mr. COATS. So the considerable amount of money spent on marketing is for that purpose; it is not directed towards the consumer?

Mr. MOSSINGHOFF. That is correct.

Mr. COATS. Those expenditures are not meant to lure the consumer from one brand to another, to lure the consumer into trying a particular drug. It is not directed to the consumer at all.

Mr. MOSSINGHOFF. That is correct.

Mr. COATS. I wonder if you could put up Chart No. 1, which was the comparison of drug prices to the consumer price index. Now, this chart is applicable to the chart that has been on display here for the whole morning, yet we see a completely different result. Can someone explain again why those two are different and what we are looking at here?

Mr. MOSSINGHOFF. What I indicated to the chairman was that the chart that the committee provided is a rate of change. It is a percent price change. We haven't looked at the data, but I assume that it is an accurate reflection of price change.

This chart is the actual dollars that you would spend or index that you would spend, and if you take that same basketful of pharmaceuticals in 1967 and give it the index of 100, if you were to buy that same basketful of pharmaceuticals today, you would pay $288. If you were to take a basketful of other consumer products, go into a store and try to buy that today, you would have to spend $331 to buy that basketful of consumer items, and it does not take into account, as was pointed out here, the improvements in technology. It is a pretty mechanistic indication of what these indices are.

Mr. COATS. I think someone indicated this rapid decrease in the blue line here in the chart on the right is primarily due to the considerable decrease in energy costs during that period of time. Is that not correct?

Mr. MOSSINGHOFF. I am not certain that that is correct. I have read criticisms of the consumer price index system in that it does weight things in the direction of energy costs and that that is a significant part of it. We could provide something for the record, if you would wish, on that.

Mr. COATS. I wish you would. With the chairman's indulgence, one final question. The implication left this morning is that drug pricing should identically track or pretty closely track the consumer price index. Is that a valid basis to determine drug pricing? What if one of your companies discovered through enormous cost and effort a cure for AIDS, but that to justify the research and development and approval and testing and marketing of the product, that caused your prices to considerably exceed the consumer price index? Would we be holding a hearing here saying you can't market that because your price increase is greater than this consumer price index?

I am not sure that we should be talking about drug pricing as a mirror image of the consumer price index, either up or down.

Does anybody want to comment on that?

Mr. WYDEN. If the gentleman would yield, I would certainly like to comment.

Mr. COATS. I would be happy to yield to the gentleman.

Mr. WYDEN. I appreciate my colleague yielding. I think what we really want to know is what are the factors that go into these prices? I would be very receptive to what the gentleman is talking about. If we could find a cure for AIDS and there were some exceptional costs involved, I would think we would want to go forward and permit those costs to be compensated in some fashion. The problem is we don't know what factors go into the prices, and in the case of AIDS, what we learned at one of our last hearings is that the price is set at random. When we tried to figure out the factors that went into pricing, we found out we were completely in the dark.

Mr. COATS. If I could reclaim my time in response to the gentleman. I think, number one, we have had some of those factors outlined to us today, and they obviously involve more than research and development. They involve product liability and a number of other things. But second, is that not what we are talking about? We are talking, in a sense, about exceptional drugs, exceptional cures that come along, that treat very small populations.

We are talking about research that takes place over a considerable period of time to bring a drug to market. We are talking about research in costs and the time factor, with no guarantee that at the end of the road, FDA approval will be granted, and that there will be one sale made of any particular drug. Yet I am sure these gentlemen at this panel could outline hundreds of drugs that are exceptional drugs, that do bring about that dramatic breakthrough in treatment, that do bring relief and treatment to maybe a very,

very small population. I just think that that incentive to develop that kind of drug needs to be retained.

Mr. **Waxman**. The gentleman's time has expired. The Chair recognizes himself to pursue some further questions.

Mr. Mossinghoff, certainly we want you to put money into research and development so we can have breakthroughs, new products, new improvements for people, but the price increases are not just on the new breakthrough drugs, they are on all the drugs that are on the market. You have already indicated that the increase in prices is in excess of the amount that is going into R&D. There are other factors in addition to R&D.

Let's put some figures on the table. Our survey showed that increases in revenues over the period of time from 1982 to 1986 came to $8.9 billion. The amount of revenue increases that came from price changes came to $4.7 billion. The increase in R&D expenditures over those years came to $1.6 billion. So we are talking about increases in prices far in excess of the increases that are going into research and development; isn't that accurate?

Mr. **Mossinghoff**. Again, Mr. Chairman, I don't know that answer to whether that $4.7 billion is before or after taxes. Obviously, that is the first thing we have to do.

Mr. **Waxman**. Let's say it is before taxes and you take taxes off. Let's say you had a 30 percent tax rate. And of course, these are only the increases. The total revenues from prescription drugs during that period of time were $64.7 billion. But the point I am trying to make is whatever other factors you want to identify, R&D costs are but a small part of what the companies are receiving by virtue of the increases in prices.

Mr. **Mossinghoff**. It is a part.

Mr. **Waxman**. It is a part.

Mr. **Mossinghoff**. It is a part. It is certainly not the——

Mr. **Waxman**. Another part is this going into marketing and detailing, and you went through some of the expenses for marketing and detailing, which do not go to the patients but to the providers of care. That would include conferences for doctors in the Bahamas. It would include flying them down on jets to the Bahamas conferences, wouldn't it? Isn't that a marketing and detailing cost? Wouldn't it include all these kinds of campaigns that now we see taking place where some companies are saying generic drugs are not safe? Wouldn't that be considered marketing and detailing expenditures as well? And, of course, there are other descriptions as you have outlined them for the marketing and detailing price increases, but those price increases have been about the same in terms of dollars that we have seen go into R&D.

What useful social purpose has been served by the millions of dollars spent by some of your members in disparaging generic drugs? Is this really a fair cost to ask the elderly consumers on fixed incomes to pay for life-saving drugs? Let me give you an example. You have an elderly person living on $700 a month, and they have to pay $100 of that for their drugs to keep them alive. Should they have to pay for a 10 percent increase per month in order to pay for the conferences in the Bahamas and the corporate jets?

Mr. **Mossinghoff**. Mr. Chairman, I don't get involved in marketing practices of our companies. I don't know about conferences in the Bahamas.

Mr. **Waxman**. I think I saw you at one. I was there, too.

That is part of the marketing expenses. The real question I want to ask you is is it fair to the elderly to ask them to pay for these increased costs, an increase that is as much going to R&D as it is going to promotion and marketing and detail men?

Mr. **Mossinghoff**. I think two of the services that the research-based pharmaceutical industry provides that are different from the generic side—and of course, as you know from your survey and have pointed out, the PMA companies do make a lot of the generic products—but two of the services performed are, first, research and development, without which there would be no new drugs, and second is educating the medical professionals about the benefits, about the risks, about the labeling that has been approved by the FDA and what that means.

So I think it is a service the industry can be proud of, this educational effort directed not at consumers but at the medical professionals. I think the doctors I have talked to since I have been in this job would indicate that it is virtually indispensable to them, the people in the daily practice, to have the sales representatives inform them, bring them articles from peer reviews about the drugs, point out what the new developments are. So I believe it is a service that the industry performs.

Mr. **Waxman**. So it is a service and we are paying more for that. Now, at some point American consumers might start feeling that they are being asked to pay too large an increase on a product they need, and they might turn to a compulsory licensing situation which is in effect in Canada, and we are going to hear more about it from Professor Eastman.

Under this kind of a system, a pharmaceutical manufacturer with patents would permit other manufacturers to produce their drug, but the original manufacturer would have to receive a royalty because it is the holder of the patent.

Now, is there anything in the Canadian system that would prevent an appropriate royalty level to guarantee funding for R&D? After all, it seems to me the biggest complaint I have heard about the Canadian system is that you don't feel the royalty level is high enough, but if the royalty level were high enough in order to guarantee new R&D expenditures, why wouldn't that be a reasonable way to proceed? Given that your members have raised prices so far in excess of their R&D needs, why wouldn't a very generous licensing system established in this country pay for your R&D while resulting still in substantially reduced prices for American consumers?

Mr. **Mossinghoff**. Let me say first with respect to compulsory licensing, there have been several, a handful, I guess, of suggestions over the 200 years of the U.S. patent system, and all of those, fortunately, have been rejected by Congress as being not the kind of system that the U.S. Government should support. We are the flagship patent system of the world, and I think the U.S. position in the world is in part as a result of that.

I honestly believe——

Mr. **Waxman**. Well, part of the position of the U.S. today is that the American consumers are paying ever-increasing prices for the drugs, and many of these people are paying it out of their own pockets when they live on fixed incomes, and a lot of them are saying enough is enough, do something about it. Now, if we want to do something about it, we have to look at alternatives. If you received a sufficient royalty from this compulsory licensing system to compensate you for the fact that you were the innovator company, we could get lower prices for the consumers and still get the amount of money we need and want for R&D increases.

Mr. **Mossinghoff**. Mr. Chairman, I firmly believe that if the U.S. were to move to a compulsory licensing provision against one industry, in this industry it would be the death knell of the research and development. I think that chart that we are very proud of that shows an exponential gain in research and development, I think you would see that nosedive the year after compulsory licensing would be enacted. I am absolutely convinced of that.

Mr. **Waxman**. I appreciate your comment. The only comment I could make in response is that if we see ever-increasing prices, then we might well have to decide as a society that we are not going to tolerate it. We want R&D increases, so we will have to specify an increase for R&D. After that we are going to have to protect the consumers, and one way to protect the consumers is a system like the compulsory licensing system so that you can get some kind of benefit from competition, and at the same time you still reward the innovator. I know we disagree.

My time has expired, and I want to recognize Mr. Wyden.

Mr. **Wyden**. Thank you, Mr. Chairman.

Mr. Shoff, I was very interested in the last statement that you made in your testimony because I think it really hammers home what I think pricing is all about. You say that pricing reflects the business environment in which we operate, and I think a lot of people have suggested that that kind of business environment is one, in effect, such as in the AIDS situation with AZT, where the consumer is essentially a captive for the industry. The customer has got to purchase drugs at whatever price the industry charges or they just suffer and possibly die.

My question to you would be: At what point in the business environment, when you are really looking at this issue, how does your concern for the customer relate to your concern for profit and your shareholders?

Mr. **Shoff**. I believe that our pricing decisions in Winthrop are not taken lightly. We are concerned with the consumer, our partners in health care. We are also concerned about the need to invest today in medicines for tomorrow.

Now, as I also had said, Mr. Congressman, that most of our products are sold through hospitals. Second, those products that are office-based, most of them are off patent at the current time.

I hope that I have answered your question.

Mr. **Wyden**. One last question for you, Mr. Mossinghoff, regarding the drug approval process. I share your view that it doesn't work well and there are a lot of improvements that need to be made, but drugs can't be approved without cooperation from the industry. One of the things that we noted in the New York Times article was that this hasn't been the case. Again, with Burroughs-Welcome and AZT, officials at the National Institutes wanted to test AZT in patients suffering from severe stages of AIDS-related complex. This was an area where Burroughs had some data. NIH wanted to be sure of the effects, and the company refused to turn it over.

My question to you would be: How can we reform the drug approval process until we can get the kind of cooperation from the industry we need so we know where we are headed. What can be accomplished with specific changes in the drug approval process?

Mr. **MOSSINGHOFF**. Let me say first, Congressman, that we appreciate your interest and your support for the general proposition of improving that. It is very important, not to PMA as much as it is to Frank Young, who is doing a fine job of trying to move that system to be more expeditious.

In terms of cooperation, since I have been at PMA, 2½ years, we have cooperated very aggressively with the people at the Food and Drug Administration. We have a board-level committee set up only to cooperate with them to try to improve the flow of information between our companies and the Food and Drug Administration. We are hopeful that we are going to begin to see the results of that effort in the data and the statistics as we look at 1986.

Mr. **WYDEN**. The point is you can say you are cooperating, but in instances such as the case of AZT, the companies are not cooperating. I just don't see how we can say the system is working where in case after case, such as the generic situation, we see disparaging comments made by some companies about generics. Or the drug approval process where all of you want changes and legislators such as myself agree that there should be changes, but the industry doesn't cooperate.

I just think there are going to have to be some dramatic changes on the part of the industry in order to drive the drug prices down. And to the extent this involves FDA reforms they must work with the Congress.

Mr. **MOSSINGHOFF**. Well, Congressman, I don't know of any drug company that would not cooperate with the Food and Drug Administration when the Food and Drug Administration asked it for more clinical data.

Mr. **WYDEN**. But here it is in the New York Times. It says specifically that the Institutes of Health wanted information from Burroughs-Welcome on the question of some of the AIDS effects, and the company refused to give it. That goes right——

Mr. **MOSSINGHOFF**. I am not in a position, obviously, to comment on the article or the accuracy of the article, but the NIH is quite different from the Food and Drug Administration. The Food and Drug Administration is the organ that approves drugs; NIH is the basic research arm of the Federal Government.

Mr. **WYDEN**. The bottom line is that the company got assistance from the Federal Government, and the Federal Government is trying to get basic information so eventually a cure can be developed, but the company is not cooperating. Until we see the effects of that cooperation, I don't think there is going to be a lot of support for changes in the drug approval process. That is why I think we have got a lot to do here if we are going to really turn some of these concerns around.

Mr. **Waxman**. Thank you, Mr. Wyden.

Gentlemen, I want to just raise a few points, and because of the limits of time, I am going to do them almost rhetorically. On the issue of liability costs as being a factor for the increases for drugs, a well-known business research organization, the conference board, published this year the results of a survey on product liability that was conducted among 232 major U.S. corporations. According to this survey, the vast majority, 67 percent of these companies, attributed an insignificant amount, 1 percent or less of their final prices to the cost of liability insurance. Certainly it is a factor, but let's don't put it out of proportion. If it is 1 percent or less, that certainly can't be that much of a factor for the increase in prices for drugs.

Now, on the issue of the cost of developing new drugs, Mr. Mossinghoff, you referred to a study that was done in 1976, sometimes known as the Hanson Study. I find that study seriously flawed in terms of credibility. Without going back and forth with you on challenging it, I just want to indicate that we are going to ask the Office of Technology Assessment to do a study to provide a more objective picture of drug development costs.

Now, on the issue of patents being long enough to recoup your costs, I was quite amazed at your statements. We extended the patent period under the Waxman-Hatch law for up to 5 years, and that is on top of the period of time. We also did a survey with the PMA of the drugs that were at FDA and how long it was taking to get them approved. The results were quite interesting.

The 50 top-selling drugs, those drugs that the companies cared the most about, averaged 14.9 years of patent time left after FDA approval. The second 50 top-selling drugs averaged 12.9 years of patent time left after FDA approval. The 100th selling drug had sales of less than $10 million a year, so the top 100 drugs include the most important drugs for the purposes of analyzing patent term.

They had a long period of time to recoup their R&D costs and make a reasonable return, 12.9 to 14.9 years. I just want to point that out more or less rhetorically because it is hard for me to accept the argument that the price increases are due to the fact that the patents aren't long enough. We have given a patent extension, and it seems to me we ought to be seeing some benefits from that extended patent period in terms of restraints on costs. That was one of the arguments the PMA made to us why we needed a patent extension. Of course, it was one of the arguments the PMA made to us why you needed an R&D tax credit.

Instead of seeing a drop in prices as a result of longer patents, tax breaks and other beneficial treatment, we see increases in prices.

Mr. **Mossinghoff**. Mr. Chairman, could I comment on that?

Mr. **Waxman**. I am going to ask you a question and then you can answer. At our last hearing in July of 1985, you described your industry's large price increases as a short-term development. You also told us that the reason we had price increases was to pay for R&D costs, and it made it seem at that time that it was R&D costs almost exclusively. Another industry witness stated at that hearing that price hikes were self correcting and this is all going to be a temporary phenomenon and that we were going to see a decrease in prices.

Since July of 1985 the CPI has risen 2.7 percent. Retail drug prices have risen 12.2 percent, a rate more than four times the CPI. Will you please tell this committee and the American consumers when they can expect some restraints from your industry on price increases?

Mr. MOSSINGHOFF. Mr. Chairman, I really don't recall saying any prediction on my part of pricing. PMA stays so far away from the pricing policies of our companies that I would not have any basis to say that, and I don't have any basis now. We really do not involve ourselves in the pricing policies of our companies.

Mr. WAXMAN. Let me ask the other members of this panel. We had witnesses, maybe not the witnesses here today, tell us in 1985 that what we were seeing was a short-term increase in prices, certainly a remarkable increase, but nevertheless one that would not continue, and instead we have seen a larger jump. When can we tell the American consumers that those kinds of price increases will no longer be facing them year after year after year, especially for those people that are on fixed incomes, and if they get an increase in their fixed incomes, it is based on an increase in Social Security, which is also based on increases in the CPI.

Does anybody want to tell us when we can expect this situation to correct itself?

[Pause.]

Mr. WAXMAN. I don't see a lot of eagerness to respond. Mr. O'Neill?

Mr. O'NEILL. Mr. Chairman, I think that is a very difficult question. I don't think it is fair for me to predict when we will have a decline in the price increases. I can tell you specifically that our price increases have gone from 8.4 percent as a percent of sales in 1982 to 4.7 percent. We have taken about a 1 percent decline per year.

I think realistically you have to give the Waxman-Hatch Bill time to work effectively through the marketplace because a significant number of compounds are losing their patentability, and they are losing anywhere from 35 to 50 percent of their total volume the first year because of the bill. I think this is going to have an impact on prices, but I can't really judge by company when this will occur.

Mr. WAXMAN. So you think somewhere in the future we may see some improvement.

Well, I just want to point out, Mr. Mossinghoff, from the transcript of the hearing that we last had in 1985 you said, "Mr. Chairman, but this short-term development should not obscure the fact that over the years, drug price increases have been substantially less than the overall rate of inflation."

Mr. MOSSINGHOFF. I was referring to the short term, I think, during the 1980 to 1985 period, and referring to the long term from the time the CPI was defined as 100. I think that is the context.

Mr. WAXMAN. I will accept your statement, but let me just say in summary that what I am hearing from you and the other members of this panel is that we are not facing short-term increases in drug prices of a phenomenal amount, we are facing it as a permanent part of what the elderly and the sick in this country are going to have to pay each year. If that is the case, then let me tell you that we are going to have to look at alternatives because that is going to be an intolerable situation, and we are going to have to look at compulsory licensing and at other kinds of restraints.

I would prefer that we not, and we would prefer that the drug industry look to see how they could restrain price increases, but we see no self-restraint, and I think the American people have to ask: if there is not going to be self-restraint by the industry, why aren't their elected officials doing something to protect them from these increases?

I thank you very much for being with us, and we are certainly going to be looking at these issues in more detail with you as we examine the whole problem facing the health care system.

We have the FDA up next, and they are coming in at 1:30. I think this would be a good time for us to break and return here at 1:30.

[Whereupon, at 12:12 p.m. the hearing was recessed, to reconvene at 1:30 p.m. the same day.]

AFTER RECESS

Mr. **Waxman**. The meeting of the subcommittee will come back to order.

We are pleased now to call forward and recognize Mr. John A. Norris, Deputy Commissioner, Food and Drug Administration, who is accompanied by a number of other people from the FDA which Deputy Commissioner Norris will introduce.

We are pleased to have you with us. Your prepared statement will be made part of the record in full. We would like to ask you to summarize that statement in no more than 5 minutes.

STATEMENT OF JOHN A. NORRIS, DEPUTY COMMISSIONER, FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES, ACCOMPANIED BY JAMES C. MORRISON, DEPUTY DIRECTOR, OFFICE OF DRUG STANDARDS; AND JEFF SPRINGER, DEPUTY GENERAL COUNSEL

Mr. **Norris**. Thank you, Mr. Chairman. I will give just a brief overview.

I am accompanied by Jim Morrison, the Deputy Director of the Office for Drug Standards, on my left, and Jeff Springer, our Deputy General Counsel of FDA, on my right.

First, thank you for this opportunity to testify before your committee. As we all know, the Drug Price Competition and Patent Term Restoration Act of 1984 made numerous changes to the way in which we review generic drugs and permit them to come to the marketplace.

Let me first acknowledge both the pioneer drug companies and the generic drug companies for the outstanding contribution they are making to the American public. We need to continue to have their support if we are going to wage the war on AIDS and other activities we are involved in right now that are so important to the American public.

We would like to address today some of the concerns that have been raised about the way in which we review generic drugs and hopefully begin to put to rest some of these concerns, at least for the time being.

Dr. Hank Meyer testified before you some months ago. He gave you approximately a 10-month report of the implementation of the Act, and I am going to talk about what has happened in the past 21 months since that report.

First of all, the fruits of our labor have been productive. We have produced some 673 ANDA approvals in that time period compared with some 350 before the Act was enacted, so the productivity has been about twice what it was before the Act.

We are also convinced that the quality of our reviews has gone up. The quality of the applications and the data they contain is of a greater nature. In the past, we only relied on in vitro examinations, and now we have human testing data available.

The attacks on our review process have really been of two principal types, and I will just summarize them very, very briefly for you. They relate to a challenge that the generic drugs approved by the FDA are not bioequivalent to the pioneer drugs, first of all, and second, that somehow the allegation goes that the generic drugs that we have been approving cause some type of harm to patients.

Let me address very briefly the first argument, the non-bioequivalence argument. We, as you know, have a test at FDA that we use in approving generic solid oral dosage drugs. It is called the 20/20 rule, and I can answer some specific questions on it when we get into questions and answers if you would like. That is a 20 percent plus or minus confidence limit that we apply, that we use to determine whether or not drugs are bioequivalent.

The allegation is, and it is a true allegation in the sense that if one just looked at the mathematics, if Generic Drug A is at the upper confidence limit and Generic Drug B is at the lower confidence limit, there would be a 40 percent differential between the two. In actual practice, however, our experience is that there is only about a 3.5 percent average difference between the various generic drugs we approve and the pioneer drug to which they are compared in the test population.

The other argument goes to the way in which we test the generic drug. We do our testing, as you know, in young, healthy volunteers. The argument is, and it is a true one, that testing in young volunteers is not the same as testing in old, sick patients; that in fact, a brand name drug or a pioneer drug, when it is tested in a young volunteer, will react differently when it is tested in a sick, elderly patient. That is a true statement.

What we have done, though, is we have compared the generic drug in the young volunteer population with the pioneer drugs used in the young volunteer population, and then we have made a very reasonable assumption, and that is, if they are bioequivalent in that single population—namely, the young volunteer population—they will also be bioequivalent in the sick, elderly population.

To date, very little evidence has been presented challenging that approach, and we are open-minded to receiving that information and taking a look at it, but to date there has been no real successful challenge to that, and we have to look at the ethical issues of testing in elderly patients and also the non-availability, really, of patients who are not on other drugs and other regimens that would compound the testing. So we have adopted this approach as the most reasonable and rational approach.

The other major attack on our generic approach has been that generic drugs are actually causing harm to patients. The theory goes something like there are various inert ingredients in the generic drug or perhaps some types of waste products or what-have-you in the drug that are actually harming patients. In every opportunity we have had to review facts about such allegations, we have either proven that the allegations were false or we have come to some type of dead end.

The first type of dead end is we could not obtain any more information; the other type of dead end is that we found a source of information, made a request that information be submitted, but, in fact, the information has not been. Again, we have been open-minded, we are open-minded, we will be open-minded on the subject, and we would welcome the submission of data, hard, scientific data that would prove one way or the other that our systems could be upgraded, but to date we have received none.

Let me stop there. Let me just summarize by saying that with an open-minded approach, we welcome submission of data that will help us to upgrade our systems, but for now we have confidence in the system and we have confidence that the generic drugs that are on the marketplace now are both safe and effective.

Thank you.

[The prepared statement of Mr. Norris follows:]

STATEMENT OF JOHN A. NORRIS

Mr. Chairman: I welcome the opportunity to be here today to testify about the current status of the Food and Drug Administration's (FDA) implementation of the "Drug Price Competition and Patent Term Restoration Act of 1984."

As you know, this statute has made significant changes in the prescription drug marketplace and in the way the FDA reviews certain drugs for commercial marketing approval. Today, I would like to bring you up to date on what we at the FDA have done over the past 31 months to implement these amendments and on the safety and effectiveness of the generic drugs being approved and marketed under them.

When FDA last appeared before this subcommittee, represented by Dr. Harry Meyer, former Director of our Center for Drugs and Biologics, the amendments authorizing abbreviated applications, or "ANDA's," for generic drugs had been enacted only 10 months earlier. We had just completed our recruiting effort and we were gearing up to handle the increased workload of ANDA's precipitated by the new law.

We are now happy to report that our efforts have borne fruit, and the productivity and accomplishments of the generic drug review team, comprised largely of the Division of Generic Drugs and the Division of Bioequivalence, have surpassed all our expectations. During the past 12 months, 673 ANDA's have been approved, most of them for generic versions of post-1962 drugs. By comparison, before enactment of the 1984 amendments the Generic Drugs Division approved slightly more than half this number, an average of approximately 350 ANDA's annually.

Not only are we pleased with the quantity of generic drug approvals, but we are also confident that the quality of data in applications that have received approval reflects the current technology in the sciences of biopharmaceutics and drug product production. For example, all of the generic versions of the post-1962 drugs in solid oral dosage form have been tested in human studies to determine bioequivalence with their brand name counterparts, while most pre-1962 generics were approved on the basis of *in vitro* or "test tube," data only.

Criticisms of Generic Drugs and FDA's Processes

Because of the dramatic impact of the new law on the pharmaceutical marketplace, interest in sufficiency of generic drugs in general and in the quality and equivalence of generic drugs in particular has intensified in the last three years. While we at FDA do not have any preference for generic drugs over brand-name drugs, or vice versa, it is difficult nonetheless for us to hear criticisms that question the safety and effectiveness of generic drugs without feeling concern for what these criticisms might imply about the scientific validity of the drug review process that allows them to be legally marketed.

We have regarded such criticism as an opportunity to reexamine our standards and processes. Over the past 3 years we have devoted considerable effort to public explanations of our ANDA review procedures and policies as they now exist and in reexamining them with a view toward their improvement and adjustment where good science and sound regulatory practice would be better served. I submit for the record some examples of documents we have prepared that outline our ANDA review procedures and policies.

Essentially, the two primary challenges we have heard regarding the safety and efficacy of generic drugs—and to FDA's ability to ensure that generic drugs are equivalent to the brand name drugs they are copying—involve (1) criticisms of our review criteria for bioequivalence, and (2) claims of actual harm alleged to have occurred to patients as a result of their having taken generic drugs. I would like to address both briefly.

Bioequivalence

Criticisms of our review criteria of bioequivalence have involved a number of arguments that we have listened to with considerable interest and introspection. After carefully reviewing our answers for each criticism, Commissioner Young and I are satisfied that our review procedures for generic drugs are scientifically sound.

Stated simply, FDA's review of generic drugs is based on a longstanding requirement that a generic solid oral dosage drug product must be shown to have a rate and extent of absorption that, from a statistical standpoint, does not differ from that of an innovator's product by more than 20 percent. Moreover, the times that the two products take to reach their maximum concentrations in the blood stream must not differ significantly.

This "plus or minus 20 percent rule" is a statistical one that refers to a level of confidence we must have that the average difference in rate and extent of absorption between a pioneer and a generic drug will not likely be more than plus or minus 20 percent among the patients who will take the generic drug nationwide. In order to have this confidence, we generally will not permit an average difference that even approaches this level in the human subjects who test the generic drug before marketing.

Even at its outermost boundary of 20 percent, the variability permitted by our requirement does not affect therapeutic outcomes. Nonetheless, arguments have been presented which are critical of the amount of variation that our "plus or minus 20 percent rule" allegedly allows in the bioavailability of generic drugs. However, these arguments tend to be hypothetical and refer to situations that have, to our knowledge, never occurred and that, in our view, are not likely to occur.

For example, one argument is that because FDA allows a variation of plus or minus 20 percent in the blood levels between the brand name and the generic products, generics may differ by as much as 40 percent from each other. In theory, this is possible. In reality, however, actual differences of that magnitude are rarely even approached. In studies we have seen, the average variation in blood levels between pioneer drugs and generic drugs is actually only around 3.5 percent.

To keep things in perspective, a difference of 3.5 percent is small compared to other variables inherent in drug therapy. For example, the United States Pharmacopoeia permits brand name and generic drugs alike to differ in potency from tablet to tablet by as much as plus or minus 15 percent.

Moreover, as I have explained, a generic drug would not be approved if the average variation between it and the brand name produced were plus or minus 20 percent during premarket tests. Average deviations of more than 10 percent between generic and brand name products have been rare.

Another argument critical of FDA's position that has been expressed about bioequivalence involves the validity of using young, healthy volunteers as subjects for bioequivalence studies. According to this argument, elderly, sick patients can be expected to absorb and metabolize the drug differently than do the young, healthy volunteers. Therefore, according to the argument, bioequivalence testing is not an indicator of how the drug will actually perform in elderly, sick patients.

It is true that the same drug will perform differently in young, healthy volunteers as opposed to elderly, sick patients. But we have seen no data to support the hypothesis that two products found by conventional tests in healthy patients to be *bioequivalent* actually produce different clinical results in patients. Moreover, there are ethical and practical reasons for testing in healthy volunteers. I'm sure we would all agree that it is preferable to subject healthy people, rather than already weakened or disabled patients, to the blood sampling and other discomforts of bioequivalence testing. Further, elderly and sick patients are usually on several medications simultaneously, confounding the analytical process and increasing variability of results. Therefore, we continue to believe that it is more appropriate to determine bioequivalence based upon testing in young and healthy volunteers than in patients.

Time concerns prevent me from reviewing every bioequivalence argument we have heard in recent years. But it is worth mentioning that Commissioner Young and I conducted a three day public hearing on bioequivalence last fall in an effort to air all of the issues related to this subject and to provide all interested parties an opportunity to comment to us. The hearing drew over 50 speakers and an audience of more than 800 scientists, lawyers, drug manufacturers, and other interested people from this country and from abroad. The published transcript is over 750 pages. We are still analyzing the transcript and the comments submitted to a public docket we created for that purpose. A Task Group appointed by Commissioner Young will report to him in the near future with its report.

That report will address material submitted to FDA after the hearing concluded as well as during the several days that it ran. Our first impression, however, was that data were lacking to support the criticisms that we heard. By the end of the hearing, Commissioner Young found the lack of data sufficiently noteworthy to comment on it publicly (and I quote):

". . . as a scientist, I was surprised with the lack of data presented. I would have expected much more. . . . I find sophomoric the concept: 'Well, it's out there but we don't know.' That doesn't cut any ice. I think you really have to approach it with a scientific analysis indicating how you develop a hypothesis and test it. . . . the lack of serious experimental data presented here was a surprise to me."

As I said, however, some material was submitted after the hearing ended. We are presently reviewing that material with an open mind and are committed to remaining open-minded should something new on this argument or on any of the other arguments come to our attention that is supported by credible data.

Claims of Harm

The second broad area of criticism involves claims that approved generic drugs have caused actual harm. For each claim of this type that has come to our attention, we have made every effort to learn the details of the claim and to analyze their significance. Typically, these claims have been made at symposia, or similar events, or through the media, but only rarely have they been reported directly to FDA.

In virtually every case where we have been able to learn the details, we have found that the initial reports were in substantial error in some way or another. In the remaining cases, we have asked the source of the allegations to provide us with details, and in no case have we received a response.

At our bioequivalence hearing, for example, practicing physicians spoke of their patients who suffered serious adverse effects from generic drugs. They promised to give us details so that we could investigate. They did not do so at the time, and when we sent them letters again asking for more facts, they did not respond. We still have yet to see a documented, verified case of a therapeutic failure caused by a bioequivalent generic product that has been approved by FDA and evaluated by us as therapeutically equivalent.

Conclusion

Mr. Chairman, we continue to believe that our review process for generic products is valid and that generics evaluated by FDA as therapeutically equivalent may be safely substituted for brand name drugs.

This concludes my formal statement. I will be happy to answer any questions you may have.

Mr. **Waxman**. Thank you for your testimony.

You feel confident that a drug that is approved by FDA, whether it is a brand name drug or a generic drug, is safe and effective, and you say that if you heard allegations that that could be proved to the contrary, that FDA would change its position.

Mr. **Norris**. Absolutely.

Mr. **Waxman**. I am assuming that your position has been taken even though you have received a lot of allegations from some of these brand name companies that the generics are not as good as their drugs. Isn't that true?

Mr. **Norris**. I would have to say that most of the allegations have come more indirectly than that. They have come through the media, they have come through symposia, they have come on occasion directly, but most often indirectly to us. As part of our ongoing effort to ensure the safety and effectiveness of the drugs being made available to the American public, we keep an open eye to what is being said about the processes we have.

I might just read to you a quote that Dr. Young made at the end of our 3 days of hearings that we had on the bioequivalence question at which we had 50 expert speakers and some 800 people in attendance. At the end of those 3 days of oral testimony, Dr. Young found that the lack of data was sufficiently noteworthy to comment on it.

He stated as follows: "As a scientist, I was surprised with the lack of data presented. I would have expected much more. I find sophomoric the concept, well, it's out there but we don't know. That doesn't cut any ice. I think you really have to approach it with a scientific analysis indicating how you develop a hypothesis and test it. The lack of serious experimental data presented here was a surprise to me."

Now, let me say that that was at the end of the oral testimony. We have an open mind still because there was written testimony submitted after the hearing which we are still evaluating, and we are expecting a report from our committee by the end of the summer. I will expect that a copy of the report come directly to you, Mr. Chairman, and to the other members of your committee.

We will retain an open mind as long as we are still analyzing the information, but to date, at least in the oral side of the hearing, there was no convincing evidence that would suggest that we should modify greatly the procedures we are using currently.

Mr. **Waxman**. Let me direct to you a simple, short question. You have already answered it in your testimony but I want you to tell us whether Americans should have any greater concerns about the safety or effectiveness of generic drugs than they do with brand name drugs.

Mr. **Norris**. There is no evidence at this point in time in our hands that we have analyzed that would suggest that you should have any greater concern about generic drugs than about pioneer drugs. Both of them are subject to the same type of rigorous review by the Food and Drug Administration, and both, at least at this point in time, we believe are safe and effective.

Mr. **Waxman**. The PMA this morning referenced an Epilepsy Institute report of problems with a generic drug. Have you looked into that case? Are you familiar with it?

Mr. **Norris**. I haven't, but Tim Morrison from my staff has, I believe. Tim, would you care to comment on that?

Mr. **Morrison**. Yes. This is, I think, typical of a lot of these kinds of allegations that are made. In it, a physician at the Cornell Medical School was cited as the source of quotes, Dr. Howard Peterson. I wrote to him last November asking him to provide us with full details. So far, we have not received a response, and this is typical, I think, of numerous such anecdotal types of allegations that, when asked for hard data to back them up or even just patient records, those are not forthcoming.

Mr. **WAXMAN**. So you know of nothing substantive to this claim that was made this morning that maybe there is a generic drug dealing with epilepsy that may be a problem?

Mr. **MORRISON**. That is correct.

Mr. **WAXMAN**. We have also heard from some folks that not only should generics generally not be substituted for brand name drugs, but generics also shouldn't be permitted to be substituted for other generics. Is there any validity to that kind of a claim? Has FDA any data to indicate that the substitution of one generic for another presents a problem?

Mr. **NORRIS**. We are open, again, to receiving hard data and scientific evidence that would suggest a better course for us to follow, but to date we have no data that would suggest that the confidence limits we have set, plus or minus 20 percent, and the experience we have had that the average variability of generic drugs is 3.5 percent from the pioneer standard. So that if we took the worst case analysis there, it would be actually a 7 percent swing. The outlier to one end would be 3.5 percent above the pioneer, and the outlier at the other end would be 3.5 percent below.

If you compare this to other variability in the regimen that physicians provide their patients, this is not a major consideration.

Mr. **WAXMAN**. Does a brand name drug vary that much in terms of bioequivalence from the original brand name drug that was approved initially?

Mr. **NORRIS**. Both within lots of brand name products and between lots of brand name products, there is some variability. I think that it does swing at least the same 3.5 percent, and again, the same confidence limits would be applied in reviewing of the appropriateness of those lots.

Mr. **WAXMAN**. This is the way I have always thought of the issue, and let me ask you or Mr. Springer or Mr. Morrison to confirm it. A brand name pioneer drug is approved by FDA as safe and effective. Then other drugs are produced to be bioequivalent to that drug which is originally approved as safe and effective. The bioequivalency test for other batches of the brand name drug is the same bioequivalency test to which you would subject a generic copy, when the patent is off and you are allowed to approve it.

Isn't the exact same bioequivalency test used for a generic drug as for a later batch of a brand name drug?

Mr. **NORRIS**. Yes, that is correct.

Mr. **WAXMAN**. So if the public is buying a brand name drug, they have to assume that you are looking at your test to see if it is bioequivalent to the original brand name drug that went through the same approval process as a generic drug.

Mr. **NORRIS**. Yes, so far, at least. Again I want to emphasize we remain open-minded on this.

Mr. **WAXMAN**. I hope you would be open-minded on all drugs if there is any question on any of them, brand name or generic. If you have any data about it, hard data, we expect you not to approve these drugs, but if you do approve these drugs, the American public is assuming that under the law, you are establishing that the drug is safe and effective and permitting it to be sold either as a brand name or a generic drug on that basis.

Mr. **Norris**. Yes, that is correct.

Mr. **Waxman**. Let me ask you something else. We have heard some suggestion that FDA has had difficulties in getting educational messages about the safety of generic drugs published in some medical journals, especially those where the publications receive enormous revenues from brand name manufacturers. Can you tell us whether FDA has had a problem in getting coverage with respect to your position on the safety of generic drugs, and if so, will you please indicate for the record the names of the publications involved?

Mr. **Norris**. I am not personally aware we have had any such difficulty. I think I ought to state for the record that there have been instances where we have felt really that parties on both sides of the issue were playing a little bit of hard ball. Let me be clear on that. On occasion there have been representatives of the pioneer field that have been playing hard ball, and representatives on occasion from the generic field that have been playing some hard ball.

What we have tried to do, particularly through our hearings, is bring light to the subject. This confusion that has existed for a period of time is not good for anyone.

Mr. **Waxman**. I agree with you.

Mr. **Norris**. It is not good for the pioneer companies, it is not good for the generic companies.

Mr. **Waxman**. In getting your information out to the public, and certainly the public we want to reach are the medical people, do you know of instances where you have had trouble getting straight information out because there is a bias by the publication that receives a lot of advertising from either a generic company, on the one hand, or a brand name company, on the other? Maybe Mr. Springer or Mr. Morrison would have more direct information.

Mr. **Norris**. I know of no instance. I can tell you this, that we have had quite a bit of success in getting the word out. Our bioequivalence hearings were one tool. The various press interviews that Dr. Young and I have had over the many months since then have been very helpful in getting that word out.

Jim, do you want to comment if you know of one?

Mr. **Waxman**. Mr. Morrison or Mr. Springer, do you know of any instances of this?

Mr. **Morrison**. I would not. I would agree with Mr. Norris that we have, I think, been pretty successful at getting the message out, both directly and indirectly, by such things as reprints of articles that we have had in certain things like the National Association of Boards of Pharmacy Newsletter, which have been reprinted widely.

Mr. **Waxman**. What you are saying is different than what I am asking. I am happy to hear that you have success in getting the message out. My question to you is, in getting that message out, have you found some avenues of publications that could further carry this message that have been closed to that information because they have advertising revenues from the brand name companies or the generic companies?

Mr. Springer, do you know of any instances of this?

Mr. **Springer**. I know of none.

Mr. **Waxman**. Mr. Morrison, do you know of any?

Mr. **Morrison**. No, I have had no experience. I know of none either.

Mr. **Waxman**. Now, a number of brand name manufacturers continue to promote blatantly deceptive and unfair anti-generic messages. Can you tell us whether you have seen any evidences of this and whether they are successful?

Mr. **Norris**. I don't have specifics in mind, but again, I can state my earlier comment that there have been occasions when both pioneering drug rhetoric and generic drug rhetoric was excessive, and that was one of the primary motivating forces for Dr. Young and I to conduct 3 days of hearings. As you probably recall, Dr. Young was quite ill during that period and, in fact, had a very bad episode at one of the hearings days. It was something that we needed to do, though, because of the rhetoric that was out there, both sides. What we wanted to do was bring light to the subject.

Mr. **Waxman**. Now, if you see any misadvertising or misrepresentation by any drug company about the FDA activities in approving drugs, do you have sufficient statutory authority to clamp down on those kinds of misrepresentations through advertising?

Mr. **Norris**. Why don't I have Jeff answer that from a legal perspective.

Mr. **Springer**. As we mentioned before, the Agency has brought to bear pressure on both sides of the issue here through our various campaigns, through the hearings and other means. We have been able to get the message out. We believe, therefore, that under the current authority, we can solve that problem.

Mr. **Waxman**. The point that we are talking about, is that it is one thing for a company to say our drug is better or brand name pioneer drugs are better than generics or generics are better than the brand name drugs. That is the sort of thing you see in competition all the time. But if someone said "my competitor's drug just doesn't really work," is that of a different kind of degree than mere competitive statements that would be permitted?

Mr. **Norris**. Let me restate your question to see if I hear it correctly. Not that my drug is better, but the other drug either doesn't work at all or, in fact, may be harmful to you if you take it, that it may have inert ingredients or other kinds of waste products that would be harmful to you.

Mr. **Waxman**. Right.

Mr. **Norris**. I personally have not seen that kind of ad out there. I do know in the instances where I have seen things or Jim and his people have seen things, we have issued a cease and desist order. I believe—and Jim, you can comment on this further—that 100 percent of the time the cease and desist orders have been complied with.

Mr. **Waxman**. You have the authority to issue a cease and desist order should there be advertising of that kind of level of misrepresentation?

Mr. **Morrison**. It is equivalent to a cease and desist order. It is a letter that goes out to the firms, and the firms have been responsive to those kinds of letters. I think that the majority of the kinds of statements that you are alluding to are made in forums that are not within the purview of drug advertising but are in the public arena that no agency has control over.

Mr. **Waxman**. I thank you very much for your testimony. We appreciate what you have had to say to us and your enforcement of the law.

For our last witness, I would like to call forward Professor H.C. Eastman, Department of Economics, University of Toronto.

Dr. Eastman, I want to thank you very much for being here. I know you have traveled a long distance, and it's not the most convenient thing to do, to come to Washington, but we very much appreciate it. We wanted to hear from you as an education for us about what the system is like in Canada, and as we look at alternatives, what some of these alternatives are like in practice.

So we are pleased to have you with us. Your prepared statement will be in the record, and we'd like to ask you to summarize that statement as you see fit.

STATEMENT OF H.C. EASTMAN, DEPARTMENT OF ECONOMICS, UNIVERSITY OF TORONTO

Mr. **Eastman**. Thank you very much, Mr. Chairman. It is a pleasure to come to talk to you about Canadian experience with compulsory licensing.

As I guess everybody knows, compulsory licensing of pharmaceutical patents simply means that under the present Patent Act in Canada, any person can go to the Commissioner of Patents and ask him to issue a license for a pharmaceutical product, even when the patent-holder will not willingly give that.

The origin of the policy is to be found in 1919 and United Kingdom legislation, partly introduced, I believe, because the British authorities found during the First World War that there were no significant British firms in the pharmaceutical industry, and they wanted to weaken the pharmaceutical patents somewhat to provide an entry for British firms.

The legislation was widely copied in British countries, including in Canada, which introduced compulsory licensing in 1923, but that was compulsory licensing to manufacture.

As you know, the patent resides in the active ingredient, which is in most cases a chemical, and the economies of scale, at least relative to the Canadian market, are such—especially were such—that it wasn't feasible for firms to obtain a license which was conditional on manufacturing in Canada. So nothing much happened.

The next stage was the inquiries in the United States and in Canada in the late 1950's and early 1960's, all of which, at least in Canada, came to the conclusion that prices of pharmaceutical products in Canada were excessively high. It was thought at the time that prices were higher than in the United States, but, in fact, I don't believe on further investigation that that was the case. Canadian prices of brand products, patented brand products, have been pretty consistently 82 to 85 percent of U.S. prices when there is no generic competition.

Nevertheless, that was the opinion, and all three of these inquiries proposed weakening patent protection in order to lower prices by having more generic competition, and that was done in 1969 when the legislation was amended to permit the importation of active ingredients.

As a consequence of that, generic firms have grown. There are four major firms, of which two are extremely vigorous and have obtained compulsory licenses for the major sellers and especially the major selling drugs that are relatively easy to manufacture. These firms—of course, I'm characterizing them in a rather sweeping way, but the general procedure is that they purchase the active ingredient overseas in countries with weak patent protection, such as—well, Italy, Israel, Hungary, Singapore, mainland China, a number of such countries—import the chemical and manufacture the final dosage form in Canada.

The result of that is or was in 1983 that the price of those drugs that faced generic competition of this sort, the multi-source drugs, were much cheaper than they would otherwise have been, and roughly speaking, if one takes as the price that would otherwise have obtained, 85 percent of U.S. prices, you find that the average price of multi-source drugs is about 50 percent of that, and that is divided between the patent-holder and the licensee, with the patent-holder's price being about twice that of the licensee. In other words, the effect on the prices of these drugs has been quite dramatic.

The total effect on the cost of drugs was estimated for 1983 to be a saving for the purchasers of drugs who are—about 55 percent individuals, who pay either directly, although there are not many of those, or through insurance premiums, private insurance schemes, and the Provincial Governments, who pay most of the drug costs for people over 65 and for people on welfare assistance of one sort or another. So the total saving for these taxpayers and consumers was about $200 million out of a total cost of drugs of $1.6 billion. So it was about an eighth of the bill that otherwise would have been paid.

Now the question then arises, well, this is a substantial sum. What has the effect been on the firms that retain patents, that hold patents?

And here if we look at the aggregate dimensions of the industry, one cannot note any correlation between the compulsory licensing and the rate of growth of the industry or the profitability of the industry. That is not to say that some firms have not been severely adversely affected; they have. But the market in general has grown very significantly because of the aging of the population and the role of provinces in funding the drug bill of the elderly, so that we have this vast paradoxical result that the overall profitability of the industry appears not to have suffered, even though we know there was a significant impact from compulsory licensing.

So perhaps I should stop there, Mr. Chairman, and answer any questions you may have.

Mr. WAXMAN. Thank you very much, Dr. Eastman.

[The prepared statement of Mr. Eastman follows:]

STATEMENT OF H.C. EASTMAN

WIDESPREAD MEASURES TO CONTROL DRUG PRICES

Most governments have instituted policies to affect the price of pharmaceutical products. Examples include profit controls in the United Kingdom, restricted lists of drugs with costs reimbursed by governments under their health plans in most European countries and the compulsory licensing of pharmaceutical patents in Canada.

WHY PHARMACEUTICAL PRODUCTS RECEIVE SPECIAL TREATMENT

The particular characteristics of the pharmaceutical industry explain government concerns that prices maybe excessive.

The quantity of drugs demanded is especially insensitive to price, because each patented prescription drug is a monopoly. The drug is prescribed by a physician who is often unaware or little concerned with drug costs. The consumer, for his part, in most cases does not pay for the drug himself, considers the drug essential to his health and lacks the knowledge to find a cheaper product with similar therapeutic effect when that is possible. As a consequence, high prices relative to the cost of manufacture can be set and, if the drug is a big seller, a lot of money is made.

The possibility of high prices and profits encourage firms to spend heavily on promotion and on research and development. On a world wide basis, the promotion to sales ratio is about 20 percent and the R and D to sales ratio is less than 10 percent.

The R and D leads to new drugs that reduce mortality and morbidity, but also to imitative drugs that do not constitute therapeutic advances, though they are costly to develop and to market.

Promotional activity provides information to physicians and pharmacists, but also encourages costly and sometimes excessive use of drugs.

CANADIAN PATENT POLICY FOR PHARMACEUTICAL PRODUCTS

In the 1960's, three major inquiries in Canada concluded that pharmaceutical prices were too high. The Kefauver hearings in the United States were reaching similar conclusions at about the same time.

All three studies recommended that the objective of lowering drug prices in Canada be addressed by modifying the Patent Act. This was done in 1969 by extending compulsory licensing to import patented pharmaceutical products. Licensees can import the active chemical ingredients and sell medicines in Canada in competition with patentees. Because of the wording of the Patent Act, the Commissioner of Patents has set royalty rates of 4 percent of the licensee's prices when granting compulsory licenses, which leads to very low prices.

THE EFFECT OF COMPULSORY LICENSING OF PHARMACEUTICAL PRODUCTS

Compulsory licensees have naturally chosen to sell generic equivalents of the major selling drugs. This has reduced the prices of these multi-source drugs significantly and achieved savings for consumers and governments that I estimated at over $200 million out of total sales of $1.6 billion in 1983. The effect of generic competition on the price of a few drugs is illustrated in the table appended, which shows the U.S. price of the patented drug, the patentee's Canadian price and the compulsory licensee's price in Canada.

VIEWS ON COMPULSORY LICENSING OF PHARMACEUTICALS IN CANADA

The policy has aroused considerable criticism from the patent holding sector of the pharmaceutical industry and of the governments of countries in which those firms are owned. Some firms have been seriously hurt by generic competition, though the industry as a whole remains very profitable. On the other hand, consumer interests, provincial governments (which pay 45 percent of the drug bill) and those who think standard patent protection is excessive are in favor.

Some Canadians also believe that the compulsory licensing policy has discouraged R and D spending in pharmaceuticals in Canada. Others simply think it improper to give pharmaceutical products weaker patent protection than is extended to other products.

My own view is that standard patent terms are not a law of nature, but that patents are an instrument of industrial policy that should be finely tuned to reach particular objectives when that is possible. To be more specific: in the case of pharmaceuticals, I believe that standard 17 year protection from the date of patent grant gives rise to excessive prices and costs unless offset by some other steps. I also think that unrestrained compulsory licensing at existing royalty rates would, if employed in all countries, probably elicit too little research. The continuation of the present regime in Canada might result in Canadians not bearing a sufficient share of world wide R and D costs.

FUTURE CANADIAN POLICY

The Government of Canada is now proposing to amend the compulsory licensing provisions of the Patent Act so that licenses will not be issued on a drug's first patent until the drug has been on the market for 10 years. A Board is also to be established with the power to revoke this 10 year exemption from compulsory licensees when it judges the price of a patentee's drug to be excessive.

TABLE 2

PRODUCT		GENERICS-(1)	BRANDS-(1)	BRANDS-(2)	EST.CDN. SINGLE SOURCE	CDN.GENERIC PRICES AS % SINGLE SOURCE	CDN.BRAND PRICES AS % OUR SINGLE SOURCE PRICES
CEPHALEXZIN	250mg	13.67	20.11	83.74	71.18	19	28
	500mb	26.92	43.52	164.57	139.88	19	31
CIMETIDINE	200mg	6.3	27.54	50.87	43.24	15	64
	300mg	7.5	23.47	53.25	45.26	17	52
	400mg	14.81	36.26	61.0	51.85	29	70
METOPROLOL	50mg	9.7	13.4	28.77	24.45	40	55
	100mg	17.8	24.2	48.77	41.45	43	58
NAPROXEN	250mg	13.0	30.0	55.2	46.92	28	64
	375mg	17.8	39.89	70.38	59.82	30	67
	500mg	25.8	69.96	86.94	73.9	35	95
CHLORAZEPATE	3.75mg	5.0	13.76	35.67	30.32	16	45
	7.5 mg	11.0	17.87	44.37	37.71	29	47
	15 mg	18.80	32.09	65.91	56.02	34	47
SALBUTAMOL	2 mg	5.28	7.50	19.63	16.69	32	45
	4 mg	8.80	13.95	29.31	24.91	35	56
	10 mg	36.88	59.85	82.88	70.45	52	85
	20 mg	63.64	100.33	138.88	118.05	54	85

(1) From Ontario Drug Benefit Formulary Dec. 1, 1986.

(2) From U.S. wholesales' purchase price list dated 01/01/87
based on largest package size, and using exchange rate of 1.38.

(3) Costs estimated based on CDN prices as 85% of U.S. prices (Eastman).

Mr. Waxman. First of all, I do want to point out to my colleagues for the record that you were the Chairman of the Commission on the Report of Inquiry on the Pharmaceutical Industry in Canada in 1985.

Mr. Eastman. You are very well informed.

Mr. Waxman. Yes. And I was impressed by your statement in the prepared views where you say: "My own view is that standard patent terms are not a law of nature, but that patents are an instrument of industrial policy that should be finely tuned to reach particular objectives when that's possible. And to be more specific, in the case of pharmaceuticals, I believe that standard 17-year protection from the date of patent grant gives rise to excessive prices and costs, unless offset by some other steps."

Now the pharmaceutical industry in this country—maybe elsewhere as well—dislikes the idea of Canada's compulsory licensing system, because they believe it does not provide them with a sufficient return in order to fund research and development.

Without passing judgment on whether Canada's system does that now, let me ask you whether there is anything inherent in compulsory licensing that would prevent an adequate return for R&D?

Mr. Eastman. Well, I think it's probably true that opinion in Canada shares the view that the present policy would benefit from modification, and the reason—leaving aside the general view and returning to mine—I think that the generic part of the industry is becoming extremely efficient, as well as having considerable resources, and the possibility then arises that generic competition would become so widespread as to very significantly erode the ability of firms to cover their costs.

My own view is that some of those costs might be reduced to the benefit of social efficiency, and that, I might say, is a view that is shared by governments elsewhere. As you know, many governments limit the ratio of sales that can be spent on promotion costs. It's not only myself who feels that the information that doctors get from the promotional activities of patentees does not require quite as much expenditures as are actually made on them. For instance, the United Kingdom limits the expenditures, or did, to 9 percent, and it's about 20 percent in Canada.

So my feeling is that costs could go down. Nevertheless, the advantage that a compulsory licensee with very low royalty rates as exist in Canada is such as to make the traditional way of doing things quite difficult, if the licensing were widespread. And as a consequence of that, I had suggested that the problem could be addressed by raising the royalty rate. The royalty rate could then reimburse the patentee who has done the research for his efforts from the—by adding to the costs of the licensee.

Mr. Waxman. Let's step back a minute and look at it from a societal point of view. Society wants to encourage research and development, innovation, production of new therapeutic agents. We want a pharmaceutical industry that is going to be as innovative as possible. It's to society's benefit to have that. And that's the whole idea of the patent law that we have in this country, that we're going to give incentives through protecting the innovator.

If we allowed immediate competition for a product that was innovated and developed, then there's not a lot of incentive to develop it, because you could just wait around and wait for somebody else to develop it. So we want to reward those people who develop something new.

On the other hand, if you have that as the permanent fixture, that they have a patent forever, it gives them an ability to have a monopoly. And whenever you have a monopoly, it's inconsistent with the free market, competitive system that produces benefits to consumers through choices. And because there are choices, if there's competition based on the price of the product, the price tends to be stabilized.

So you try to balance off these two things, and the way that we have balanced it off in this country is we give the patent for a period of time, and we say, "You have a monopoly during that period of time, but when that time is over, we want competition." So then we allow generic drugs to compete.

Another way of providing that balance is to say, "If you're the innovator, you have the patent, but that doesn't keep others from producing the drug. It means that if they do produce the drug, you are to be rewarded, because you are the patent-holder." If you are rewarding the patent-holder and still allowing competition in the sale of the product, you are obviously reducing the value to the patent-holder, compared to what we have in this country.

If you do that, do we run the risk of driving the industry out of the area of trying to be innovative and creative and produce more breakthroughs?

Mr. **Eastman**. Well, it's hard to judge how an industry—how members of an industry would respond to a major change in the way in which their intellectual property is handled. But in principle, there should be no—there should be an equivalence in terms of the return to the inventor as to getting his income from the royalty on a product manufactured from others or from having a monopoly right of his own which excludes competition, and hence he gets a return from the higher price that can be set in the absence of such competition.

My personal view is that compulsory licensing, as a general system, not simply for this industry, is a valid one. It's especially relevant to this industry, because it's one which is particularly vulnerable to generic manufacturing. Duplicating an invention is easy, once it's been made, compared to many other industries.

Mr. **Waxman**. Well, I guess going back to your statement, "Standard patent terms are not a law of nature; this is a decision by society and society's representatives have to decide what is in the best interests of the public, both for innovation and for consumers."

Now the people who purchase drugs or need drugs in Canada don't generally purchase them themselves. They usually have a health care system that purchases the drugs. Isn't that the case?

Mr. **Eastman**. Yes. About 45 percent of the population has its drugs paid, to a very substantial extent, by provincial governments. I guess another 45 percent is covered by some kind of insurance. A few of the plans, of these private plans, are so-called generic plans where the insurer requires the product that is bought to be generic. And then 10 percent of the population buy their own drugs without that kind of protection.

I might say that the sale of generic products is also encouraged by the provinces, and each province is a little different, but at least Ontario and Quebec and some other provinces will only reimburse at the lowest price. So whichever drug is dispensed by the pharmacist, the price is normally that of the generic manufacturer.

Mr. **Waxman**. That's a function of the health care system in Canada. But one of the functions of the health care system in the United States is that the consumers who need the drugs must pay for them out of their own pockets, for the most part. Overwhelmingly, they are not reimbursed by Government-funded insurance programs or private insurance programs for most of the pharmaceuticals that are purchased. And it seems to me that that is an argument for those looking at the present situation for drug pricing in this country to say, maybe there's a greater need to change the balance that the society must try to accomplish between giving the incentives for innovation, but yet not pricing people out of the ability to buy those drugs they need to survive—or if not pricing them out, putting such a tremendous burden on them.

You know, what we really have is a shift of wealth from people who are the least able to bear these costs to an industry that shows the highest return on its investments. So you have a shift, a completely regressive shift, from people on the lower income side to corporations on the higher income side. We are elected to look at what the public interest should be in this country and might have to ask whether it makes sense to have that kind of shift of wealth for a basic, essential ingredient such as pharmaceuticals.

From the point of view of the Canadian system and your recommendations for changes in the Canadian system, you would achieve that balance through a different way than the way we try to achieve it here.

Mr. **Eastman**. Yes. I would not venture an opinion about the U.S. system, since I don't really know the conditions in the United States sufficiently well, but those were my recommendations for Canada. As is often the fate with a commission, they were not accepted in substantial part, and what the Government is now posing is to keep compulsory licensing, but in a modified form, by protecting the patent for a longer time. For most patents, it would be for 10 years after the clearance for marketing of that drug.

Now that will only be for the first patent on the chemical, so that any subsequent patents taken on the same medicine will still be subject to compulsory licensing.

Mr. **Waxman**. They're looking at a proposal to move more in the direction of the United States' system; is that——

Mr. **Eastman**. I beg your pardon?

Mr. **Waxman**. In Canada, they are looking at a proposal to move more in the direction of the United States' system.

Mr. **Eastman**. Yes, that's the case. At least to extend the patent protection. But it has these two wrinkles. One is that it's only on the first patent. The second is that the period of exclusivity, which is superimposed on the patent of 17 years, is calculated based on the moment when the drug is put on the market. So that if you had in the 10 years in addition to the lapse of time from the patent grant to the clearance for marketing, which might be another 6 or

7 years, the total term will be only slightly shorter on the whole than the first patent.

Mr. **Waxman**. Is your government looking at this change in order to encourage more innovative pharmaceutical research-based development in Canada?

Mr. **Eastman**. That is the bargain that the Minister has announced, that in discussions with the Pharmaceutical Manufacturers Association of Canada, the Association has promised the—I guess a quid pro quo, that the R&D to sales ratio would go to 8 percent in 4 years and 10 percent in 10 years, which would be a very substantial increase over the historical level in Canada since 1969.

Mr. **Waxman**. So in Canada they're looking at a bargain where every 10 cents out of a dollar will go to R&D under this new proposal?

Mr. **Eastman**. For every 10 cents on sales, yes, which is approximately the worldwide R&D ratio for the major firms in Canada, now operating in Canada, or at least was in 1983.

Mr. **Waxman**. And consumers will pay a dollar more in Canada to get 10 cents more for R&D?

Mr. **Eastman**. No. No, no. I don't think it will work that way. It's very difficult to calculate, and I have not been in a position to do so, to estimate what the additional cost of drugs may be in future from this new policy.

The principal reason for that is that it applies only to new drugs, and we don't know what they are, and hence it's very difficult to estimate. But I would be very surprised that the cost change would exceed the R&D change in dollar terms.

Mr. **Waxman**. Well, Canada and the United States are very different countries, although we have much in common. And as it respects this kind of balancing that we both are trying to achieve, in some ways, as you look at it from different perspectives, you might say the grass looks greener on the other side of the fence.

But when I hear about the fact that consumers can benefit from lower prices, and still there can be innovation for development of new drugs, that strikes me as an attractive alternative to one where there is a monopoly, and the consumers are faced with such a large bill.

I wouldn't want to endorse such a system, because I'm not sure of all of the ramifications for this country, although I think this is something that we have to think about because there is a balance to be achieved, and when things are out of balance, then what we have is a system that is unfair, either to the goal of innovation or unfair to the objective of allowing consumers to buy drugs they need.

I appreciate your being with us to give us some kind of insight into a system that we haven't really looked at that carefully in this country, but perhaps we will have to look at with greater care to see if that may be one of the alternatives to get us out of the very difficult situation we are in today.

Thank you very much.

Mr. Eastman. It was a pleasure to come.

Mr. Waxman. That concludes our hearing today. We thank all those who participated in it, and we stand adjourned.

[Whereupon, at 2:28 p.m., the hearing was adjourned, subject to the call of the Chair.]

MEDICAL DEVICES AND DRUG ISSUES
FDA's Implementation of Medical Device Amendments of 1976

MONDAY, MAY 4, 1987

House of Representatives,
Committee on Energy and Commerce,
Subcommittee on Health and the Environment,
Washington, DC.

The subcommittee met, pursuant to notice, at 10 a.m., the Hon. Henry A. Waxman (chairman) presiding.

Mr. Waxman. The meeting of the subcommittee will come to order.

At the outset I would like to mention for the record that Mr. Sikorski has informed us that although he has a strong interest in this hearing and would have appeared if he possibly could, he has a long-standing commitment that conflicts with this hearing and prevents him from being here. We regret his absence and look forward to working with him on medical device issues in the future. [See p. 391.]

Also for the record, the two major trade associations whose members sell medical devices, the Health Industry Manufacturers Association, HIMA, and the National Electrical Manufacturers Association, NEMA, have indicated that they do not wish to present testimony today.

Most Americans know that the Food and Drug Administration regulates drugs. Because of FDA, most of us believe that the prescription drugs we use are as safe and effective as can reasonably be expected. Many people don't know it, but FDA also regulates medical devices, products that can be anything from bedpans to x rays to pacemakers. FDA's authority over devices makes perfect sense. Like prescription drugs, medical devices are very special products and require special scrutiny for safety and effectiveness.

For example, any medical devices are implanted into the body, and they carry out lifesaving functions and often remain more or less permanently.

However, unlike prescription drugs, most medical devices today manage to escape effective regulation. As we will see in this morning's hearing, only a handful of devices that Congress has directed FDA to approve for safety and effectiveness have actually been so approved.

What does this mean for those of us who must be treated with medical devices? Well, it means that we have to ask some troubling questions.

For example, what happens when a medical device is inside your body and turns out to be defective? Frankly, the answer is not encouraging. A defective medical device presents unique problems. As difficult as it may be to identify and recall defective consumer products, such as an automobile or a child's toy, it is far more complicated to deal with potentially dangerous artificial joints or pacemakers or heart valves. Dangerously defective implants have to be removed and replaced.

Unfortunately, this can mean major surgery with all of its attendant risks and suffering. Even devices that are not implanted can present enormous hazards.

In my own family I have seen the unfortunate life-threatening consequences of problems associated with medical devices. That experience is a vivid and continuing one, one that has certainly heightened my sensitivity regarding today's hearing.

Clearly the best approach is to have a system that provides reasonable assurances that medical devices are both safe and effective before they become a routine part of medical practice. There is a law that is intended to provide such assurance. That law is the Medical Device Amendments of 1976. It was passed in order to give FDA authority over devices similar to that which it has over drugs.

Under the law, high risk devices require approval by the FDA before they can be sold. Other devices that present serious but lower risks require performance standards promulgated by the FDA. All other devices must conform to FDA's general controls, such as its good manufacturing practices.

Although the law seems fine in theory, in practice it has never worked. Unfortunately, a loophole in the law has allowed most medical devices to escape effective regulation. Under the loophole, manufacturers simply claim that their new devices are substantially equivalent to old devices, those that were on the market before 1976. Most manufacturers resort to this approach variously described as the 510(k) process, premarket notification, or substantial equivalence.

On this point I direct your attention to charts set up in this room, also included in the memo we sent to the subcommittee's members.

As you can see, we used the term "premarket notification" in the charts. We could just as easily have said substantial equivalence or 510(k). Well over 98 percent of the new devices that enter the market each year do so by claiming substantial equivalence, rather than going through premarket safety and effectiveness reviews.

Under the substantial equivalence approach, devices that come onto the market 50 years from now will have to demonstrate only that they are as safe and effective as devices on the market before 1976.

Even today, technological improvements have rendered obsolete many medical devices that were on the market 10 years ago when this law was passed. Yet new devices claiming substantial equivalence need not incorporate these improvements. They need only be as safe and effective as devices on the market over a decade ago.

What this means is that Americans continue to serve as guinea pigs for new medical devices; and what's worse, once a device in the market proves itself defective, there's no guarantee that FDA will even learn about the problems, let alone get the devices off the market.

As we will hear, the system to report defects is itself defective. One of the major arenas for medical device use and injuries is hospitals. Yet hospitals don't have to, and therefore don't, report medical device hazards to FDA.

Moreover, FDA's recall powers are extremely narrow under current law and don't permit the agency to take quick action unless manufacturers cooperate.

Unfortunately, not all manufacturers do cooperate.

In closing, let me state that I think the problems are clear. What we need are solutions. Last year we suggested some legislative changes that we thought would help reduce the problems. We continue to refine this legislation. To do this properly, we must have the cooperation of consumers, manufacturers and the FDA. And if it takes more hearings like this to ensure that cooperation, then we will hold more hearings.

Today we will hear from a number of witnesses who have had troubling personal experiences with medical devices. We believe that their stories will help illustrate the points we have made this morning. But before calling on those first witnesses, I want to recognize the very distinguished Chairman of the full Energy and Commerce Committee, and also the Chairman of the Subcommittee on Oversight and Investigations, which has played an active role in looking at the medical device problem, Mr. Dingell.

Mr. DINGELL. Mr. Chairman, I thank you. I commend you for holding these hearings. I believe they are very important. I am here primarily in my capacity as Chairman of the Subcommittee on Oversight and Investigations.

As you know, Mr. Chairman, for the past several years the subcommittee has conducted numerous hearings and investigations relating to problems with specific medical devices and with the Food and Drug Administration's implementation of existing medical statutes.

Mr. Chairman, your hearings this morning are a testament to the manner in which oversight and legislative processes are intended to work. Under the Rules of the House, it is the responsibility of the Oversight and Investigations Subcommittee to review and study the application and administration, execution and effectiveness of laws within the jurisdiction of this committee, and to determine those laws and programs which should be continued, curtailed or eliminated, and to report on a need for new or additional legislation.

In this matter, Mr. Chairman, your subcommittee is carrying out its responsibilities in a very appropriate fashion this morning, and I commend you and the subcommittee for the work you are doing, and I want to express my particular appreciation for the way in which our staffs have worked together on this particular matter.

Some brief studies of the way the Subcommittee on Oversight has worked for the past few years, I believe, would be useful to the record.

In 1982, the subcommittee conducted its first hearings regarding implementations of the 1976 Medical Device Amendments. The testimony was received from the Commissioner of Food and Drug and from outside public interest groups. Those hearings examined FDA's activities with regard to a number of medical devices, including contact lenses, tampons, and something known as a volumetric pump cassette.

In May of 1983, the subcommittee issued a report entitled "Medical Device Regulation: The FDA's Neglected Child." The inescapable conclusion of the subcommittee in that report was that FDA's performance in the implementation of medical device amendments is a picture of bureaucratic neglect for public health and safety that is indeed shocking to the conscience.

Indeed, at that point FDA barely had begun to implement the provisions of the law which had been enacted more than 6 years previously. Some of the specific findings of the committee contained in that report include the following:

One, through negligence or by intention, the FDA has failed to implement the major provisions of the Medical Device Amendments of the Food, Drug and Cosmetic Act.

Two, FDA is relying almost exclusively on general controls to regulate devices when it previously determined that such general controls were inadequate.

Three, as a consequence, FDA is unable to assure the American public that many medical devices currently on the market and relied upon to treat disease and sustain life are safe and effective.

Four, by failing to restrict devices to address problems caused through their misuse by inappropriately trained persons or poorly equipped facilities, FDA has failed to deal with the most frequent source of device-related injuries.

Five, FDA seriously compromised the credibility of its law enforcement deterrence when, having found clear violations of law, it failed to recommend meaningful prosecution promptly and vigorously.

The subcommittee's report also contains a number of legislative recommendations to address these problems. The subcommittee hearings conducted in March of 1984 focused on failed pacemaker leads and on FDA's faulty administration of the law that contributed to these problems.

The subcommittee hearings were conducted, examining anesthesia machine failures in September of 1984 and, once again, FDA was faulted for its failure to properly and promptly implement the provisions of the 1976 laws.

One might ask, is there anything positive that can be said about FDA's implementation of the 1976 medical device amendments? In my assessment, the answer to that is clearly yes. After 6 years of total neglect for this legislation, I believe that FDA has begun to demonstrate good faith attempts to implement major provisions of this 1976 law. They have yet to be totally successful, for a number of reasons.

One reason is that to implement the letter of the 1976 law would entail enormous undertakings in terms of time, money and personnel, which parenthetically are not currently available to that agency because of budgetary constrictions and because of the actions of OMB.

The second reason why FDA has yet to fully implement the provisions of the law is their genuine belief that some of the provisions are more rigorous than necessary to ensure safe and effective medical devices. That may be correct, and FDA might be right in some regards. I believe that we are here this morning because most of us concluded that this law is not perfect in every particular.

Mr. Chairman, our constitutional form of government, the Rules of the House, the oaths of office taken by all of us, allow for limited options with regard to discharge of the responsibilities. Very fully, our oversight responsibilities require the full and faithful execution of laws. If it is determined that there are deficiencies in existing laws, our responsibility then is to amend those laws. There exists no option which provides for an agency to determine the adequacy of existing laws and then to vary the implementation of those laws according to the whim of the agency.

There is one message that I would like to leave very clearly with the subcommittee this morning. We will either amend this law or we will ensure its proper implementation. Congress, and particularly any subcommittee or committee which I chair, will not tolerate de facto amendment or repeal of any law by any executive agency. That is a function of the Constitution which requires that the Congress take such action, and that is a function and responsibility which this Congress will carry out, and it will not be carried out by executive or administrative fiat.

All of us are to be assured that the Oversight Subcommittee will continue a full degree of interest and activity to ensure FDA's proper execution of the law. The Oversight and Investigations Subcommittee reported what we believed to be a number of inadequacies with the existing law. You are familiar with the work of the subcommittee, and I greatly appreciate again, Mr. Chairman, the way in which our staffs have worked together and the cooperation that you and I have shared as we have looked into matters relative to Food and Drug law.

I would observe, Mr. Chairman, I am not committed for or against any legislative proposal. I believe that your subcommittee can deal with this matter with full competence and full adequacy. I am open to any particulars that may be developed by your subcommittee, and I am anxious to observe the record that you will develop as you begin the hearings this morning.

I reiterate, Mr. Chairman, I commend you for initiating the process, and I will look forward to working with you to ensure that any amendments to this legislation that you would bring forward will receive the most careful and full consideration in the Full Committee. I am satisfied that they will protect the health and safety of the American public, and I commend you for your labors this morning.

Thank you, Mr. Chairman.

Mr. **Waxman**. Thank you very much, Mr. Dingell. I want to commend you on an excellent statement. Without objection, I'd like to add to the record the memorandum for members of the subcommittee.

[Testimony resumes on p. 348.]

[The memorandum referred to follows:]

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MEMORANDUM

To: Members of the Subcommittee on Health and the Environment
From: Henry A. Waxman, Chairman
Re: Medical Device Hearing, May 4, 1987

On Monday, May 4, 1987, the Subcommittee on Health and the Environment will hold an oversight hearing on the implementation by the Food and Drug Administration (FDA) of its authority over medical devices.

Like prescription drugs, medical devices are highly specialized consumer products. In many cases, medical devices are surgically inserted into the body and are intended to remain there permanently. As difficult as it may be to identify and recall an automobile or children's toy, it is far more complicated to deal with a potentially defective or dangerous artificial joint or pacemaker or heart valve that has been implanted into someone. Clearly, the best solution is to have a system that provides reasonable assurance that the devices are both safe and effective.

There is a law that is intended to provide such assurance. That law, the Medical Device Amendments of 1976, is complex. In order to place the issues in perspective, this memo describes relevant sections of the law and provides some background information on FDA's implementation of it.

The Law

Before 1976, FDA had limited authority to take action against unsafe or ineffective medical devices. Although the agency could seize devices or enjoin their sale after their introduction into commerce, it could not, with extremely limited exceptions, take action against devices before they entered the marketplace. This narrow authority over devices stood in sharp contrast to FDA's broad premarket authority over drugs.

Recognizing that FDA's authority over medical devices was inadequate, and acknowledging the number of deaths and serious injuries identified with medical devices, such as the Dalkon Shield, Congress in 1976 amended the Food, Drug and Cosmetic Act to expand FDA's powers dramatically. Under the 1976 device amendments, Congress directed the agency to establish a three-tiered regulatory scheme:

-- Class III devices require premarket approval. Before these devices can be sold, manufacturers must submit specific documentation to FDA demonstrating that the devices are safe and effective;

-- Class II devices require performance standards. Before they can be sold, these devices must comply with safety and effectiveness standards promulgated by FDA;

-- Class I devices, although requiring neither premarket approval nor performance standards, must conform to FDA's general controls, such as its Good Manufacturing Practices (GMP).

Congress did not "grandfather" devices in the 1976 law. Rather, the law requires FDA to regulate all devices -- whether marketed before or after 1976.

In addition, the law provides FDA with explicit "recall" authority for medical devices. Under appropriate circumstances, the agency can seek the remedies of repair, replacement or refund. This recall authority is similar to that of other health and safety agencies in some respects. In one respect, however, FDA's recall authority with regard to medical devices differs substantially. Under the device amendments, FDA must not only prove that a product is dangerous, it must also demonstrate that at the time the device was designed and manufactured, it failed to meet "the state of the art as it existed at the time of its design and manufacture."

Oversight Hearings

In May, 1983, the Subcommittee on Oversight and Investigations issued a report on FDA's implementation of the medical device amendments. The report, titled "Medical Device Regulation: The FDA's Neglected Child," found that, notwithstanding the clear mandate of the law, FDA had yet to regulate a single preamendment device (i.e., a device on the market before passage of the 1976 law) through premarket approval. Similarly, the report found that the agency had yet to promulgate a single performance standard for any device -- preamendment or postamendment.

Instead, according to the report, the FDA devoted the bulk of its regulatory efforts to two categories of devices. The first is the so-called "transitional" devices, i.e., those devices that FDA, prior to 1976, had convinced a court to treat as drugs and thereby to require premarket approval. The second is Class III devices introduced into the market after 1976.

FDA's approach meant that all devices on the market prior to the 1976 law (so-called "preamendment devices") could remain on the market even where the agency had found that they were potentially dangerous enough to require either premarket approval or performance standards in order to ensure their safety and effectiveness.

Moreover, the report concluded that by allowing all preamendment devices to avoid the full degree of regulation mandated by Congress, FDA opened a loophole for most post-1976 Class III and Class II devices to escape regulation as well. Under the loophole, manufacturers of post-1976 devices can simply claim that their devices are "substantially equivalent" to pre-1976 devices and enter the market without having to go through premarket approval or meet performance standards. These post-1976 devices can be sold until FDA regulates the pre-1976 devices to which they claim "substantial equivalence."

The Expansion of "Substantial Equivalence"

Section 510(k) of the medical device amendments requires manufacturers who propose to introduce new devices into interstate commerce to notify FDA prior to doing so. All such devices are considered to be Class III devices -- and therefore are barred from sale without premarket approval -- unless they meet certain exceptions. As noted above, the largest exception is when a new device is "substantially equivalent" to a pre-1976 device for which FDA has not yet required premarket approval or for which the agency has not yet promulgated a performance standard.

This exception has virtually consumed the rule. As noted above, until regulated by the FDA, any pre-1976 device and all post-1976 devices substantially equivalent to the pre-1976 device may be sold to the public without restriction. Given that FDA has not regulated any pre-1976 devices, most manufacturers resort to this approach, variously described as "the 510(k) process," "premarket notification," or "substantial equivalence." As demonstrated in Chart One in this memorandum, well over 98 percent of the new devices that enter the market each year do so through premarket notifications claiming substantial equivalence rather than through premarket approvals.

These large numbers have been made possible not only by section 510(k), but also by FDA's extremely broad reading of the section. As interpreted by FDA, section 510(k) permits post-1976 devices that have the same intended use as a pre-1976 device to enter the market so long as they are as safe and effective the pre-1976 device.

Under FDA's approach, devices that come onto the market fifty years after passage of the law will only have to demonstrate that they are as safe and effective as devices on the market before 1976. Even today, more than ten years after the law was passed, major technological improvements have occurred with many medical devices. Yet, under FDA's 510(k) approach, new devices need not incorporate these improvements; they need only be as safe and effective as similar devices on the market before 1976.

The most important implication of this broad application of the 510(k) process is that the vast majority of medical devices now entering the market are only minimally scrutinized for safety and effectiveness.

FDA's approach led the Oversight Subcommittee to state in 1983,

> ... by defaulting in its obligation to establish safeguards for classes II and III devices, the agency has forced itself to rely heavily upon the 510(k) process as a weak surrogate mechanism to provide some modicum of assurance of the safety and efficacy of devices that, contrary to congressional intent, are subject only to general controls.

The Current Situation

Very little has changed since the 1983 Oversight Subcommittee report. As illustrated in the attached charts, no premarket approvals for pre-1976 devices have been completed, no performance standards have been promulgated and most new devices still reach the market through section 510(k) premarket notification.

As also illustrated by the charts, the number of reports of potentially defective medical devices and of device recalls has *increased substantially* in recent years. In part, this reflects the promulgation by FDA of mandatory reporting requirements at the end of 1984. Whether there are other reasons for the increases in hazard reports and recalls will be explored at the May 4 hearing. Whatever the reasons for the increases, it seems clear that Congress should be concerned about whether the public is being adequately protected under the current system.

Explanation of Charts

Chart One: This chart illustrates that less than 2 percent of the new devices that come onto the market actually do so as a result of premarket approval (or as a result of complying with safety standards). Rather, most devices simply rely on premarket notifications, i.e., "substantial equivalence" determinations pursuant to section 510(k) of the law. In these cases -- constituting 98 percent of the new devices entering the market -- FDA permits the devices to be sold to the public without approving them for safety and effectiveness.

Chart Two: This chart illustrates that most of the new products entering the market fall within Class III or Class II. Although FDA is congressionally mandated to regulate these devices with premarket approval and performance standards, in fact -- as illustrated in the charts in this memorandum -- FDA has failed to do so.

Chart Three: This chart illustrates that roughly 3 to 7 times as many Class III devices get onto the market each year through premarket notifications (i.e., "substantial equivalence" determinations pursuant to section 510(k) of the law) as do through premarket approvals by FDA. As stated above, premarket notifications permit devices onto the market without FDA approval for safety and effectiveness.

Chart Four: This chart illustrates that FDA has not completed a single premarket approval proceeding for a Class III device that was on the market before passage of the medical device amendments. The roughly 140 pre-1976 Class III categories contain approximately 1,000 separate medical devices produced by device manufacturers.

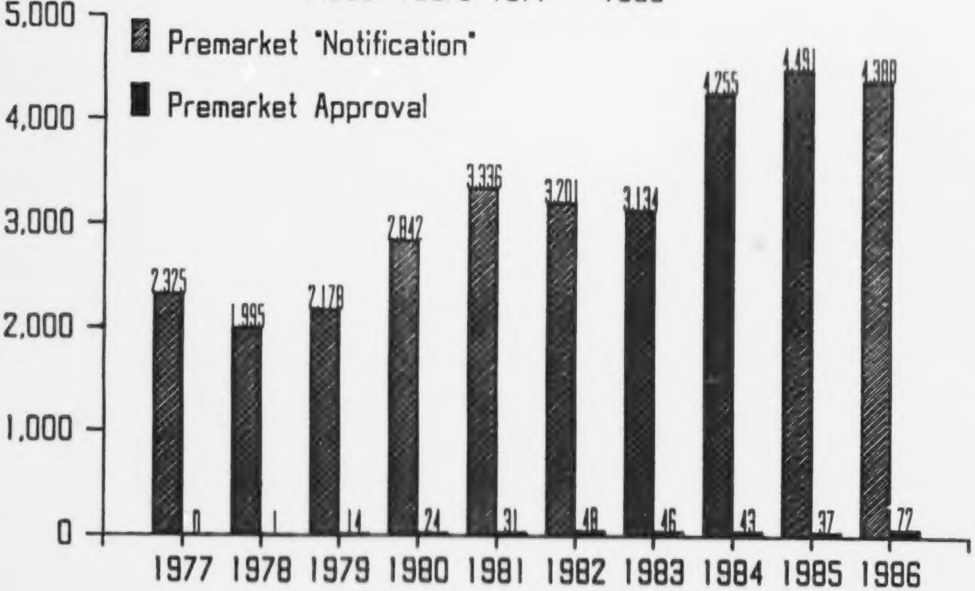
Chart Five: This chart illustrates that FDA has not completed a single performance standard for any of the devices classified by the agency as requiring performance standards in order to be considered safe and effective. The roughly 1,100 Class II categories contain tens of thousands of separate medical devices produced by device manufacturers.

Chart Six: This chart sets forth the number of reports received by the FDA identifying medical devices that may have caused or contributed to a death or serious injury. The chart shows the number of reports received under the DEN system, which is voluntary, and the MDR system, which is mandatory. Before FDA promulgated the MDR rule, many manufacturers argued that a voluntary system adequately reported potential hazards associated with medical devices. FDA rejected that argument. The number of reports to FDA under the mandatory system have run at a rate almost six times the best rate of the voluntary system.

Chart Seven: This chart sets forth the number of recalls recorded by FDA involving medical devices. Although many manufacturers insist that the current premarket approval and standards-setting process at FDA works well and needs no changes, these data suggest that Congress should be greatly concerned about whether the public is adequately protected.

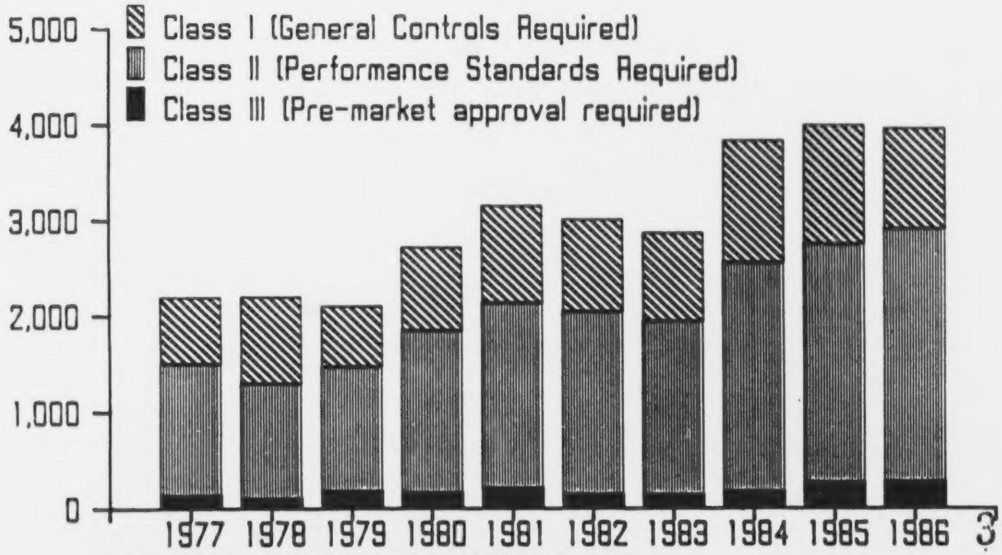
How Medical Devices Reach the Market: Premarket "Notification" versus Premarket Approval

Fiscal Years 1977 - 1986

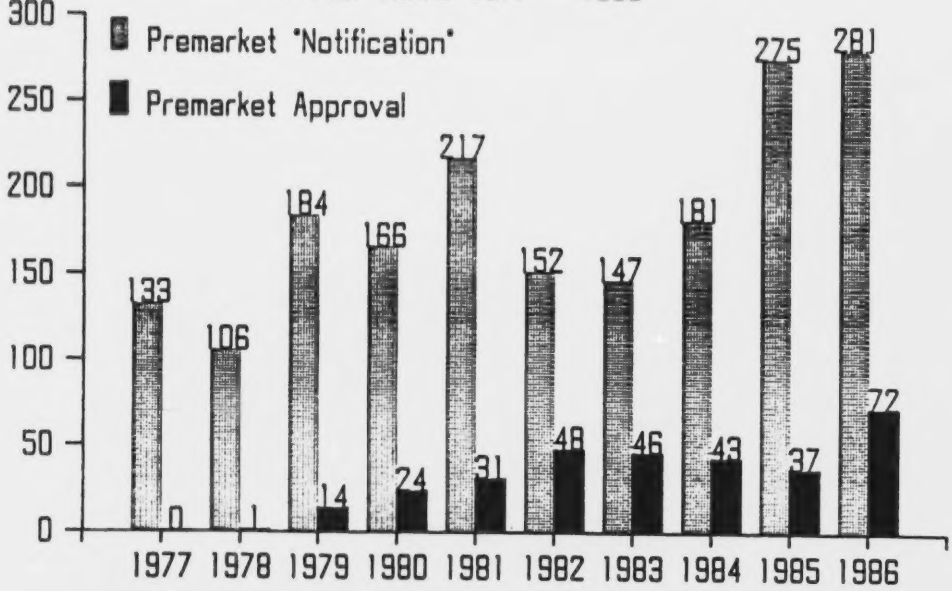


Number of Medical Devices, By Class,* That Reach the Market Through Pre-Market "Notification"

FY77 - FY86

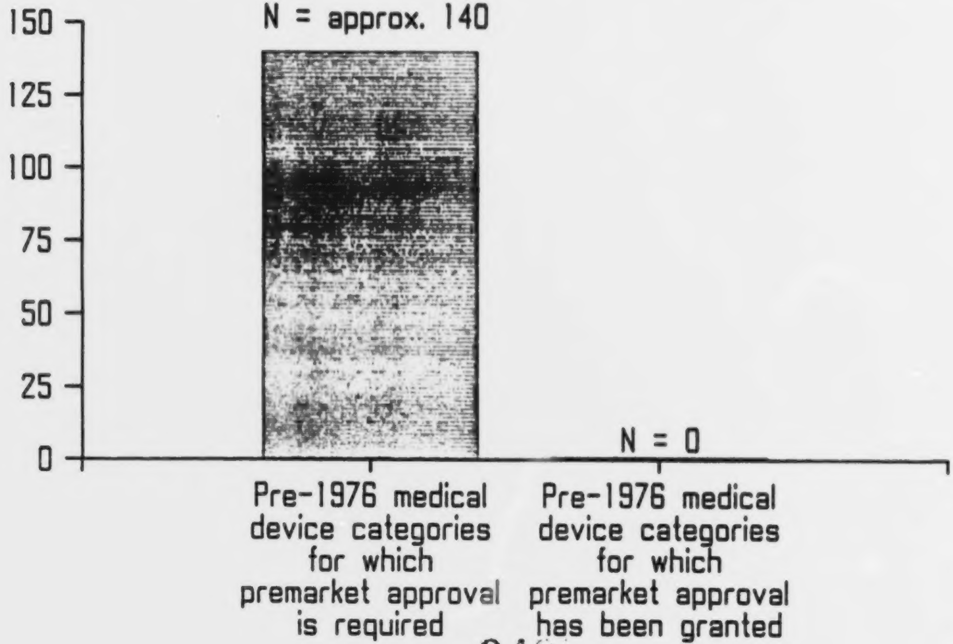


* Chart excludes a small number of devices designated as "no class."

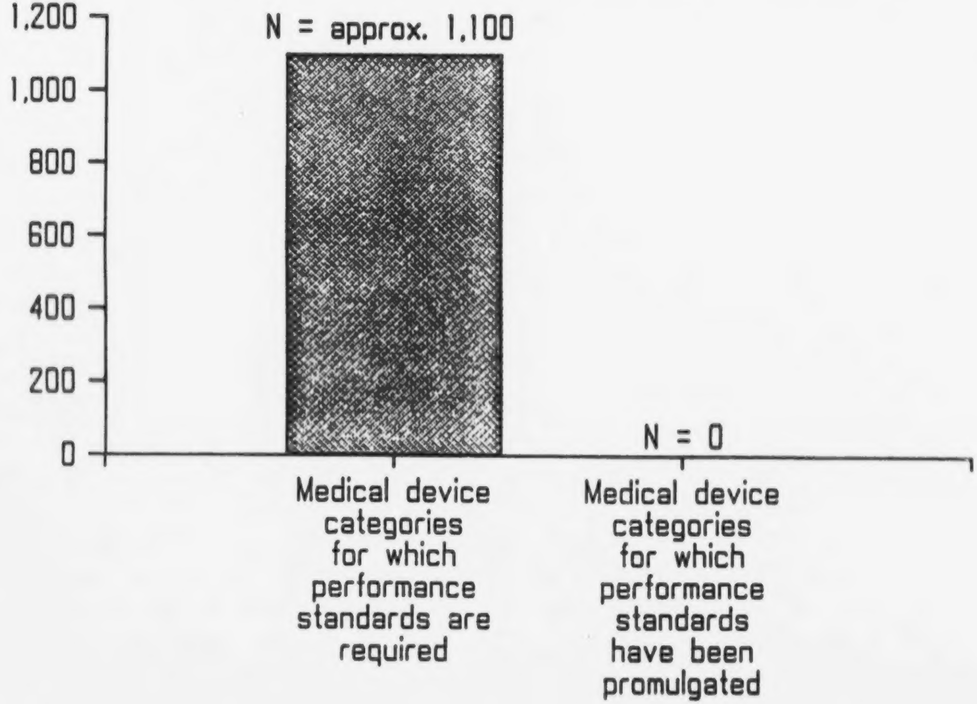


How Class III Devices Reach the Market:
Premarket "Notification" versus
Premarket Approval
Fiscal Years 1977 - 1986

Backlog of Pre-1976 Class III Premarket Approvals

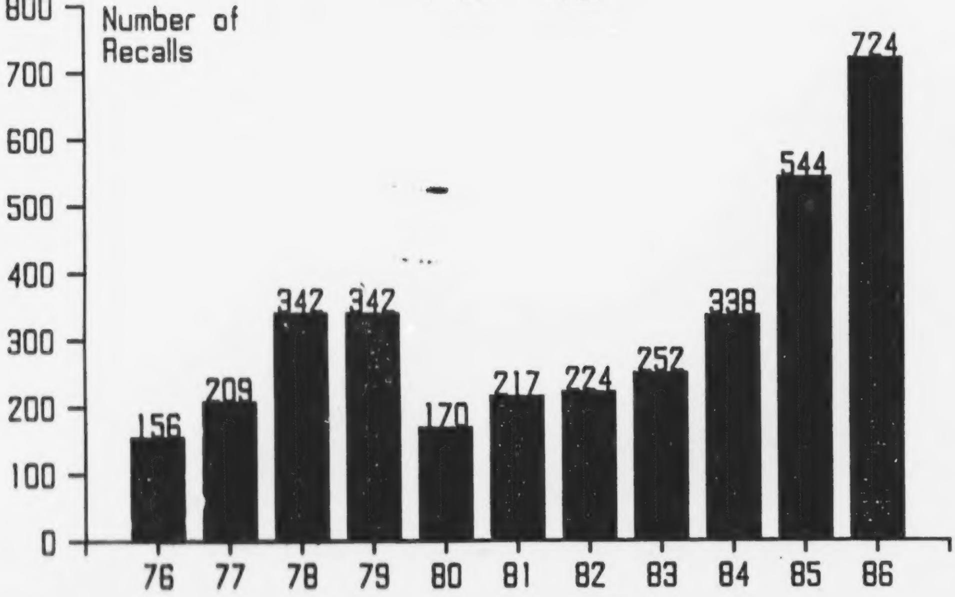


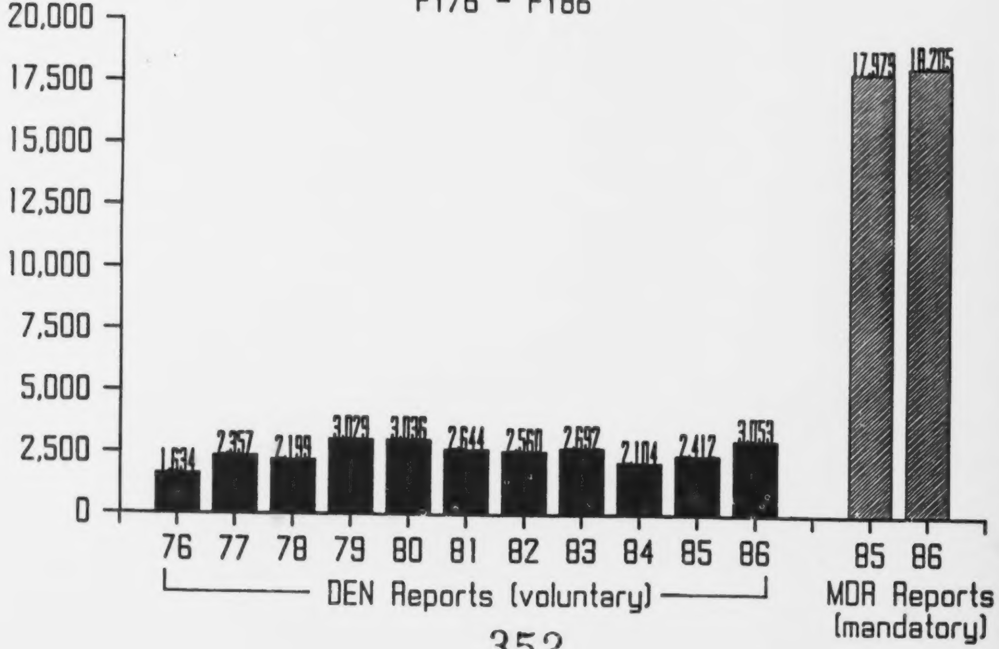
FDA Performance Standard Backlog



Number of Medical Device Recalls Per Fiscal Year

FY76 - FY86





Reports to FDA of Potential Hazards Associated with Medical Devices
FY76 - FY86

Mr. **Waxman**. I would like to call our first panel to come forward to this table. Will the panel of Pam Taylor, Clayton Burger, Anna Burger, Tama Jackson, James Jackson and James Young please take seats at the table, if you would.

We want to thank you very much for coming before the subcommittee this morning to tell us about your experiences with medical devices. Although we obviously can't make any kind of judgment as to claims you have against manufacturers involved, we think your experiences illustrate the potential for harm involved when we are talking about a medical device in the current regulatory system.

We would appreciate if you would tell us about your situation and try to keep it to around 5 minutes so we can hear from all the witnesses today.

Ms. Taylor, why don't we start with you. If you would just pull that microphone closer to you, and then there's a button at the base, just push the button.

STATEMENTS OF PAM TAYLOR, MILLBURY, OHIO; TAMA REASONER JACKSON AND JAMES JACKSON, WASHINGTON, DC.; AND CLAYTON LEWIS BURGER AND JULIA BURGER, BALTIMORE, MD

Ms. **Taylor**. Good morning. My name is Pam Taylor, and I would like to introduce you at this time to my daughter, Jessica Taylor.

Mr. **Waxman**. Hi, Jessica.

Ms. **Taylor**. She is the reason we are here today.

Incidentally, we are originally from Tecumseh, MI, and we have come here today from Millbury, Ohio, and I think Jessica is going to go with her uncle now so that I can be very frank with you about her experiences.

At 15 months of age, Jessica had a viral myocarditis, which apparently caused second and third degree heart block. On October 26, 1982, a bipolar pacemaker system was inserted, using two Medtronic unipolar leads, which were attached to the outside of Jessica's heart.

Eleven months after the pacemaker was inserted, Jessica blacked out on three occasions at home. She was hospitalized and subjected to repeated painful tests, and her pacemaker was readjusted almost daily for close to a month.

The problem was that her pacemaker was sensing heartbeats that weren't there, so it wasn't firing, and it was also not sensing her own heartbeats and firing inappropriately.

After several consultations with the manufacturer's representatives, the pacemaker was replaced on October 10, 1983. At that time doctors found one of these unipolar leads, which were Model No. 4951, was not functioning and it was capped off, though it was not removed from her body.

A unipolar pacemaker was inserted and attached to the one remaining lead.

We are currently involved in a lawsuit with Medtronic, and we contend that the Medtronic lead, Model 4951, that was used in Jessica's initial surgery was defective in design in the same way as another Medtronic model, Model No. 6972. This defect caused a malfunction in the pacemaker system and we do have written expert testimony to that effect.

Since the surgery we have found that the lead Model 4951 that Jessica's life depends upon was approved through the 510(k) method. Medtronics sent a letter to the FDA stating that the Model No. 4951 was substantially equivalent to other Medtronic models, specifically No. 6972.

Because of this 510(k) approval, Jessica's leads were allowed to be placed on the market without ever being tested.

On June 15, 1984, the Model No. 6972 was recalled. This was due to a defect in design that caused problems substantially equivalent to those Jessica experienced.

We also contend that Medtronics was well aware that these problems existed with their Model 6972 when the Model No. 4951 was attached to Jessica's heart.

Jessica was 2 years old when her pacemaker was replaced. She still remembers the mask that was placed over her face, and I still remember the look on her face when they took her from my arms into surgery. She still wakes up screaming. She still sleepwalks. She still has unexplained fits of anger and depression, and I still wonder every morning when I put her on the school bus, is that one remaining, untested Medtronic lead going to get her through another day. And what will I tell my 5 year little girl if something happens to that lead. God forbid. Will she be around for me to tell her anything.

Jessica was very proud that she got to come here today. She even had thoughts that she might meet the President. How can I tell my daughter that the manufacturers and the governmental departments don't care enough to test these products before they allow them to be used?

I am alarmed and I am disappointed that no one told me about this 510(k) method of approval when Jessica needed her surgery. And I am distraught when I hear about the thousands of Medtronic leads that have failed, and I wonder how many fail and go unreported. But most of all, I am heartsick that this continues to happen.

Any product that affects the health and well being of any individual must be extensively tested before it receives government approval. You have the authority to protect us. Jessica has suffered enough. She is too young to personally ask for your help, so on behalf of my daughter and the countless other victims I appeal to your sense of decency and ask that you please give this matter your immediate attention.

Thank you.

Mr. **Waxman**. Thank you very much, Mrs. Taylor.

Please tell Jessica that the fact that she came here with you gave us information that we hope will mean that we can make sure that devices for everybody in the future will be as safe as possible, and it's been very helpful to hear about your personal experiences.

Ms. **Taylor**. I will.

Mr. **Waxman**. I'd like to now ask to hear from Mr. and Mrs. Jackson.

STATEMENT OF TAMA REASONER JACKSON AND JAMES JACKSON

Mr. Jackson. Thank you very much, Mr. Chairman and members of the committee.

Both my wife and I will speak. I will try to make it very brief.

Our case involves a malfunctioning incubator. In 1981, our son, 8 days old, was literally cooked to death in a local hospital. We are very fortunate that we have two very beautiful children now; however, it does not subtract from the incident and the gravity of that particular incident.

The incubator had serious defects. The thermostat did not function properly. It was improperly placed, and the placement caused it to break and, in particular, in our case, the on/off switch did not work. It would sometimes register off when it would, in fact, be on. There were a number of other defects that were involved in our particular case.

It would overheat. It would read sometimes 100 when, in fact, it would be close to 105 or 110, and that is how our child passed.

That was in 1981. To this day, we're not sure whether that incubator is still on the market or not.

As a parent of two very beautiful children, a daughter who is about to be 1 and a son who is about to be 5, I set guidelines. I set guidelines for them, so that hopefully one day they will grow up to be very beautiful adults.

I know that my son would prefer to police himself. He is a budding diplomat. He feels that anything is negotiable. He would also like to name his own punishment. Unfortunately, that cannot happen. As well, it cannot happen on a larger scale. In our case as well, the hospital felt that they should police themselves, and they did not have—they did not have any type—method of actually working on the machines, of just safeguarding the machinery. There was absolutely none whatsoever.

That's all I have to say. I'm sorry.

Mrs. Jackson. We are nervous, as you can tell. This is not something that we enjoy doing, having to recount and relive the nightmare of watching your son die in your arms on Father's Day. We are here because we know that that incubator is mass-produced, and that it is out there humming in its deadly way in thousands and thousands of hospital rooms throughout this country and because that particular incubator is such an essential part of the hospital experience.

You have a newborn. They said, "Congratulations, Mr. and Mrs. Citizen. You have a beautiful baby. It's going to be down in the nursery. You and your family can see it when you want to." When you go and you look at your newborn child, or if you're fortunate enough your grandchild, the first thing you see is, you see the baby in the incubator.

What happens if that incubator is not safe? What happens if, as in our case, the safeguards supposedly designed into that incubator are not there, they're not functioning properly?

An incubator will overheat, as it did in our case. There is a safeguard to alert the staff that this incubator is overheating. It did not work. This incubator overheated to a temperature of 105 degrees. Imagine being in a closed container, an oven if you will, with nothing to alert someone that you need help.

What happened in our case was that someone noticed that the child—that the incubator had overheated; they opened the portholes, they took the baby out, they sponged him down, and then they put him right back in the same incubator. And unfortunately lightning struck twice. The incubator overheated again. And no one knows how long our baby laid in that incubator before someone found him.

What we do know is that when they found him, there was blood on the pillow, and his system had literally been boiled from the inside out, and there was nothing that they could do. The next 18 hours were spent in a futile attempt to save his life, and there was—his life was beyond saving, and all of which could have been prevented, had attention been paid to the maintenance, to the design, and to the care of a piece of equipment that is used so widely and is such a given in a hospital situation.

Why we are here before you today is to ask you to cast your eye in that direction also. Look at the machines that are not only in the body, but are around the body, especially a child's body.

They can't plead for themselves. We're here to plead for ther When my children grow up and they see our first pictures, I wo like to be able to tell them that this was your brother, and they will know that he is no longer with us, but I would like them to also know that because of his sacrifice, that changes were made that ensure that other children and other families will not have to undergo our particular nightmare.

Thank you.

Mr. **WAXMAN**. Thank you very much for sharing that information with us.

As I understand if, this particular incubator was on the market prior to the 1976 device law. When we checked with FDA, this is what we understand——

Mrs. **JACKSON**. Yes.

Mr. **WAXMAN**. Prior to the 1976 law. But under that law, FDA was supposed to set performance standards.

Mrs. **JACKSON**. Yes.

Mr. **WAXMAN**. And they still haven't set performance standards, and a new manufacturer can come out with the same incubator and put it on the market because it's substantially equivalent to the one they've never even gotten performance standards on.

Mrs. **JACKSON**. Exactly.

Mr. **WAXMAN**. It's a maddening situation to contemplate and understand that the risks are as great as what you had to go through.

Mrs. **JACKSON**. It's frightening.

Mr. **WAXMAN**. I would like to hear from Mr. and Mrs. Burger.

STATEMENT OF CLAYTON LEWIS BURGER AND ANNA JULIA BURGER

Mrs. **BURGER**. I'm Mrs. Burger, and this is Mr. Burger, and we came here to explain to this committee about the episode that has happened to my husband.

In the first place, before I go any further, his life is totally dependent on a pacemaker. He has no heartbeat. He had his first implantation in February of 1977. It was installed; he came home; he went to work in 2 weeks. He worked 8 years with that pacemaker with no problem whatsoever—none. And he ran heavy equipment.

In January—on January 29, 1985, the doctor decided to change that pacemaker because the batteries were running down. He installed it on the 29th, and from the minute that they installed that pacemaker and they brought him back from the operating room, I turned to the doctor and I said, "Doctor, are you sure you put the right pacemaker in him?"

He was very pale, and he didn't look good. And he said, "Well, don't forget, he's 8 years older." We accepted this.

I brought him home, and he was having these episodes of passing out. Either the pacemaker stopped, or it would skip or whatever. I kept bringing him back to the hospital. They kept telling me it was fine, because it would right itself, and they couldn't find any problem, and they told me it was recycling.

This went on from January until April. We were going away to Gettysburg, and a couple days before we left, I sent him over to the hospital. He had another one of these episodes. I sent him over to the hospital. They assured me nothing was wrong with the pacemaker and for me to go away; it was just recycling.

We went to Gettysburg on April 19, and on the 20th, he was sitting in a lawn chair talking to his sister, and he keeled over. Luckily we had a nurse about two campers away from us. She ran over; she took his pulse. It was dropping. Already it had been 42 before they had even sent for the ambulance. And when the ambulance came, the paramedics worked on him. They brought him to the Gettysburg hospital.

In the meantime, he had revived again. It had started again. And the doctor advised us to keep him in the hospital overnight, so they could check it. While he was sleeping, the pacemaker totally went out, and he went into syncope, and the way it was explained to me was that he died. There was no oxygen or anything to the brain.

And they rushed him to the operating room and called me to the hospital and told me not to come alone. They had him in the operating room, and they put a temporary on the other side.

When they called Baltimore, Baltimore insisted that they bring him back here, and so they got a special ambulance with nurses and paramedics to bring him back here, and they were supposed to take him in the operating room.

In the meantime, in the hospital, I heard that they were sending a man from California from the Pacemaker Systems, Incorporated that was supposed to sit through this operation and see what happened and to bring the pacemaker back to California. So they didn't operate on him until Thursday.

Now his type of pacemaker was the pulse generator type, an EV09109M, Model 242096. The serial number was 13692. That Thursday, they took him in and completely put a new pacemaker in him.

Since that time, whether damage was done already or whether we are still having problems with this pacemaker, but he is in and out of the hospital for the past 2 years, and we have heard nothing from the pacemaker people. We have heard nothing from the hospital. We have heard nothing from the doctors of what could have caused this pacemaker to fail.

And this is why we're here, because if they were covered, you know, by the FDA, they couldn't get away with this. They would have to tell people like us, when the doctor comes to us and tells us we have to put a pacemaker—we don't ask these questions: Has it been through—checked through FDA, or anything else, because we don't know until the damage is done.

So therefore this is the reason why we came here, and we hope that there are better regulations, because I don't know how many people have had this happen to them, or if the damage will ever be corrected for the rest of his life.

But we're hoping that someone else wouldn't have to go through this. It's a trauma, especially for the person that's going through it.

Mr. WAXMAN. Thank you.

Well, I certainly agree with you. No one should have to go through that. You should expect that someone in Government is checking these things out to be sure they're safe before they're sold.

Pacemakers are, in this medical device law, considered Class III, which means there has to be an approval before it's marketed, and under the loophole of the law, a pacemaker, if it's like some other pacemaker that's already on the market, can just be bootstrapped on, so that there's no premarket scrutiny of it, other than just establishing it's the same as the other one. And that's evidently the case with the pacemaker that was put into your husband.

I hope the result of your testimony, all of your testimony, and this hearing will lead to stronger legislation, so that we can be sure that we make the Food and Drug Administration have a law they can live with and work with, so that we can give the public the assurances they need.

We have for the next presentation something on the video. What we're going to see is, Constance Walters will present testimony by videotape.

Although Mrs. Walters indicated a strong desire to fly here to present her remarks live and would have done so, if we had agreed, we felt it would be better not to put her through the strain, given her physical condition.

Before we play the tape, let me explain a little bit more precisely what the circumstances of Mrs. Walters' case are.

Mrs. Walters was in an auto accident when she was a child. As a result, she developed over the years what is called angulation or curvature in her back. To remedy it, she had an operation in which the device she complains about, called a Weiss spring, was implanted in her back. As we understand it, about 3 months after the operation, the spring snapped.

Although I think this will be clear from the tape, I want to make sure that no one confuses her injuries from the auto accident, which led to the installation of the medical device, with her problems with the medical device itself.

Could we have the tape?

STATEMENT OF CONSTANCE WALTERS

[Videotape shown.]

Ms. **Walters.**—and I didn't realize [inaudible].

Interviewer. And that was fine with you?

Ms. **Walters.** Yes. It was—I didn't think anything, if it was fine or wasn't fine. I was just treated like I was before the accident. If there was something that I honestly could not do, they would do it for me, but I had to show them, I had to try to do it first.

Interviewer. Did you learn to cope with this injury; is that what you're saying? You learned to cope with it?

Ms. **Walters.** [Inaudible]. I never went through depression—well, I used to could walk, or I can't walk now. The only thing, I was kind of shy about getting out in public. But my parents treated me like I had no injuries, so I didn't really think of it [inaudible].

Interviewer. Please tell me some of the things you could do with this handicap. Did you drive a car?

Ms. **Walters.** I drove my own car. I cleaned house. I vacuumed. I worked in the yard. I got down on the ground, and I worked in the yard in the flowerbeds.

Interviewer. Did you——

Ms. **Walters.** I went fishing.

Interviewer. Did you go to school?

Ms. **Walters.** I went to school. I went to college, and I worked and went to college full-time at the same time.

Interviewer. Did you get a degree?

Ms. **Walters.** An Associate Degree.

Interviewer. You got married; is that correct?

Ms. **Walters.** I got married.

Interviewer. You had a child?

Ms. **Walters.** I had a child. I did everything. I could work on my car. I depended—see, the main thing is, I was independent. Now I'm [inaudible]——

Interviewer. What happened that caused you to become dependent?

Ms. **Walters.** When the springs was put in my back, from that point to now, I've been dependent on my family, on anybody who could help me.

Interviewer. What happened? What did the springs do?

Ms. **Walters.** They broke in my back in a very short time after they were put in. They caused terrible pain.

Interviewer. Did you lose any function as a result of these springs breaking?

Ms. **Walters.** I had bowel and bladder control up until [inaudible] when the springs were put in. I don't do my housework like I did before. I don't travel like I did before. We used to go all the time, anywhere, it didn't matter. We went camping.

Interviewer. And now you've got a child; is that right? How old is he?

Ms. **Walters.** He's almost 12.

Interviewer. And how has this changed your life with your child and your husband?

Ms. Walters. We don't go out like we used to on vacations. If there's a school function, my husband goes instead of me. I stay home. This is my life, in this house here.

Interviewer. You're living on disability. You get how much a month?

Ms. Walters. My total disability is $360 a month.

Interviewer. And I understand your husband gets a little bit of money from being in the National Guard.

Ms. Walters. Yes.

Interviewer. And they just recently gave him a raise?

Ms. Walters. Yes.

Interviewer. And the effect of the raise was to cut you off of food stamps; is that correct?

Ms. Walters. Yes. Now we make too much money to be eligible for food stamps.

Interviewer. And your total income is how much a month?

Ms. Walters. It's approximately—it's around $800 a month. [Inaudible.]

Interviewer. OK.

Ms. Walters. He gets a check because I get a check.

Interviewer. And then the total is how much now?

Ms. Walters. Oh, the total of all of our checks is around $800 a month.

Interviewer. And your husband can't work [inaudible]; is that true?

Ms. Walters. That's right. If he goes to work, my—it's not so much the check, [inaudible]. The other part of the disability, [inaudible], I'm getting. If John goes to work, [inaudible] he has another insurance card that helps with my Medicare insurance.

Interviewer. Let me go to something else now. These springs, are these the springs that were placed in your back, these little kinds of springs like this? Would you show them to the camera, so people can see what it is or what it was that broke?

Ms. Walters. These are the springs. They were put in about the middle of February. I got out of the hospital about 5 weeks later toward the end of March. By April, I knew there was something wrong with my back. It was not surgery pain that I was having in my back.

Interviewer. Now, Ms. Walters, if you had known more about these springs when they were put in your back, would you have had this surgery and had these springs inserted?

Ms. Walters. No, I wouldn't have. If I'd known this was more of an experimental type [inaudible], there is no way I would gamble with what my life that I had and take a chance that it would get worse. And it's worse now. I can't be anybody. [Inaudible.]

If there was some kind of guarantee and it had been done before, and there were good results, and there was years and years of tests done with these springs, then I might have [inaudible].

My life now is ruined. I used to enjoy life, and now I'm just—I cannot wait for the day to end. I can't sleep. When I lay, my back hurts. I'm in constant pain 24 hours a day, 7 days a week, 365 days a year. There's no relief.

Interviewer. Is there anything any other doctor could do to help you?

Ms. Walters. No.

Interviewer. So you're asking the people who will see your tape to appreciate the dangers of this kind of device?

Ms. Walters. Do something so someone else's life isn't totally ruined like this. It's a crime. It's an absolute crime to ruin someone's life like this.

[Witness emotionally distraught.]

[Videotape projection concluded.]

Mr. Waxman. We checked with the FDA about the specific regulatory status of this Weiss spring. As we understand it, the spring is manufactured by Zimmer, Inc. It's a Class III device but has never gone through premarket approval. According to what we can determine, the device in question was designed and manufactured in 1976 shortly after passage of the Medical Device Amendments. The manufacturer has never sought nor has FDA ever granted a determination that the device is substantially equivalent to a device manufactured before passage of the law.

This means either that the company believes that this device is so similar to a pre-1976 device that no notification to the FDA is necessary in order to market it or the manufacturer simply chose not to inform the Agency. In either case, the same point remains. This is a device that should have gone through premarket approval but never did.

Is James Young here yet? Mr. Young is to testify and I think will be arriving in a while.

For those of you that are here, we are deeply indebted to you for sharing with us your personal experiences so that we can learn from them, benefit from them, and make sure that others are spared. Thank you very much for being with us.

Thank you, Mr. and Mrs. Burger, Mrs. Taylor.

Our next witness will be Dr. Sidney Wolfe. Dr. Wolfe is with the Public Citizen Health Research Group. We are pleased to welcome you to our hearing. Your prepared statement will be put in the record in full. We would like to ask, if you would, to summarize it in no more than 5 minutes.

Dr. Wolfe.

STATEMENT OF SIDNEY WOLFE, DIRECTOR, PUBLIC CITIZEN HEALTH RESEARCH GROUP

Mr. Wolfe. Thank you, Mr. Waxman, for the invitation to appear here. In preparing for the testimony, I re-read testimony we gave 12 years ago during the legislative hearings that led to the passage of the Device Amendments. The striking thing I remember about those hearings was that instead of having the real victims that caused the hearings to occur in the first place, the more typical kind of witnesses were the potential victims if the Government regulated.

There were surgeons and companies complaining that if we had Government regulation, as one surgeon said, their creativity would be stifled, they wouldn't be able to invent the kinds of devices they needed to.

Many of the problems that have arisen since the passage of the law were clearly anticipated in 1975, when we testified and the same was true for others. We were very worried not enough devices would be put in Class III. We insisted then that it should include all life supporting devices, all life sustaining devices, all implantable devices and others.

You've heard this morning some life sustaining devices were not put in Class III but instead in Class II.

Unfortunately, the roads to increased regulation in the areas of health and safety are always paved with victims. When the number of such victims reaches a critical threshold, action occurs. One hundred people, including many children, died from the antibiotic elixir sulfanilamide, which had been manufactured using the untested toxic chemical, diethylene glycol, as a solvent. Thus, the 1938 Drug Safety Law requiring premarket testing of new drugs came into being.

The tragedy of thalidomide, the drug for pregnant women which caused severe birth defects, short, flipper like arms, precipitated the passage of the 1962 drug laws which strengthened the safety provisions and for the first time, required substantial evidence of effectiveness.

Dozens of people injured or killed by defective heart valves and the sterility and infection causing disaster called the Dalkon Shield, eventually damaging thousands of women, were major factors leading to the passage of the 1976 Medical Device Amendments.

It is insufficient, however, just to pass such laws for several reasons. First, as clearly seen during the passage of the Device Amendments, important consumer protective provisions are killed due to industry pressures. Second, after passage, continued pressure from industry and delay and inadequacy of regulations and enforcement by the agency, such as FDA, further cripple the intent of those members of Congress who wanted maximum consumer protection.

I remember that during those hearings, you, Mr. Chairman, were on the side of the consumer, trying to get the law passed in a stronger way, and I think both you and I felt that something had gone amiss when it went somewhat in the other direction and it is unfortunately even clearer now that is the case.

When serious defects in the original laws or their implementation become apparent, it is time for Congress to intervene with the passage of strengthening amendments and more vigorous oversight of FDA. Now, 11 years after passage of the amendments, the time for such action is long overdue.

I will discuss several of the most serious problems.

The first is what will have to be called nonexistent standards, in which the law says there are three classes but in fact there are two. When the people classifying devices were asked, put the devices into one of three classes, labels, standards or premarket approval, they assumed there actually were three classes. In fact, there aren't. Over 1,100 medical devices including many which are life supporting and when they fail have caused deaths, have been classified as Class II devices, the category requiring mandatory standards. This equals two-thirds of all devices classified. In 11 years, FDA has not promulgated a single standard for any of these 1,100 devices.

Mechanical ventilators are a frightening example of this regulatory negligence. A ventilator is a device that assists a patient's breathing by supplying oxygen through a tube or mask. Since it is often a life supporting device, failure of a ventilator to function properly can have tragic results. premarket testing of this device should therefore be required. However, FDA placed this device in Class II, the standards category, so that premarket testing for safety is not required, nor as mentioned above, is there a mandatory standard.

Since the 1976 Device Amendments were passed, ventilators have been the subject of 23 separate recalls. Six were called Class I recalls, this is a different classification, Class I recall meaning "there is a reasonable possibility that the use of or exposure to the violative product will cause serious, adverse health consequences or death."

During the phase of the voluntary reporting, the Device Experience Network received 290 reports of problems with ventilators and their component parts since 1976. Included were 12 deaths and 8 serious injuries including brain damage, cardiac arrest and bilateral pneumothorax, air leaking out of the lungs. Problems have included leaks in valves and tubing, separation of component parts and alarm failure.

As noted above, ventilators are Class II devices. However, there is no mandatory FDA regulatory standard for ventilators but only a voluntary industry standard is in effect.

In a little noticed part of the GAO study, which you will hear much more about, the sole cause of the often life threatening device problems documented by the surveyed hospitals was a design flaw or design characteristic in 19 percent of the cases and defective components 22 percent of the time. In the absence of mandatory FDA standards for any device or the much more preferable course of premarket testing, as I'll mention in a minute, such findings are not surprising. Many devices now in Class II such as incubators, ventilators and many more, should be placed in Class III by strengthening the law.

The next serious problem has already been referred to briefly and GAO called it "equivalent creep" in their report. It is the 510(k) fiasco. It is perhaps the biggest loophole in FDA's regulation of medical devices.

This procedure requires the manufacturer to notify FDA when it plans to market a device the manufacturer believes is substantially equivalent to a device that was on the market prior to the effective date of the Device Amendments. FDA is supposed to determine if the device is substantially equivalent or if it is a new device and must go through premarket testing. However, this decision is made without reviewing safety and efficacy data for either the new or old device, even if they are Class III devices.

According to the most recent data, most of these devices placed in Class III, those otherwise which would have required premarket testing, have been allowed on the market with merely the cry of "substantially equivalent."

In 1986, as I think this chart shows, 209 of 281 Class III devices, 74 percent, were stamped "substantially equivalent" by FDA. As a result of these wholesale exemptions from testing requirement, many devices such as pacemakers, which you heard about this morning, and other implantable devices have caused preventable deaths or injuries. When a sufficient number of deaths and injuries occur, it becomes clear that "substantially equivalent" was a euphemism for substantially more dangerous.

Further contributing to the superficiality of the 510(k) review is the lack of safety and efficacy data for the pre-enactment device that the newly marketed device is supposed to be equivalent to. A manufacturer's claim that its device is substantially equivalent to an old device can therefore only be evaluated in terms of what the device is supposed to do and how it is supposed to do it. Since FDA often has no data, the performance of the two devices, including their safety and efficacy, cannot be compared. Yet, when Congress passed the Medical Device Amendments, a comparison of safety and effectiveness was supposed to be the guiding principle of the 510(k) process. Substantial equivalency was not intended to be "so broad as to refer to devices which are intended to be used for the same purposes as marketed products."

In summary on this point, we believe that the FDA's interpretation of section 510(k) and in particular its interpretation of the "substantially equivalent" position is contrary to the Medical Device Amendments. However, because a lawsuit challenging FDA's interpretation of this provision, which we are considering now, would probably take several years to reach a final resolution and because in any event, the outcome of such a lawsuit is never certain, it is imperative that Congress amend the statute to close this loophole.

The final category has to do with mandatory device reporting by hospitals as well as industry. Although the mandatory requirements, which have now been in effect since 1984, will clearly increase the number of device problems reported to FDA, to more than the tiny fraction the GAO found, much more is clearly needed. Since such a large number of the worst device related problems occur in hospitals, we believe that the law needs to be amended to require all hospitals to report all serious device problems to FDA.

Currently the mandatory reporting requirement only applies to the manufacturer and as GAO has pointed out, not even to some of the distributors.

This addition would greatly increase the flow of reports of deaths and injuries to FDA and shorten the time it takes to find out about dangerous devices.

In summary, there are serious, death and injury causing defects in the design and enforcement of the 1976 Medical Device Amendments. Things are clearly better than they were in 1976 but as the victims we have heard this morning have implied, it is not good enough. There is no question that FDA could use more funding and more guts to better enforce these important amendments. It is equally clear that in some respects, the law is just not strong enough.

Thank you.

Mr. WAXMAN. Thank you very much, Dr. Wolfe.

As you have indicated, you strongly question the current approach that FDA takes in regulating these devices. Is it just the case that this is an agency that can't do its job or is it the case that its mandate needs to be changed?

Mr. **Wolfe**. I think there is some of both. I do believe that the panels, the outside advisory panels that were convened even before the amendments were passed, really believed when they placed something in Class II, that standards would be forthcoming. I don't think if you asked any of them they would believe today's situation in which over 1,100 standards have been recommended, and no standard has been promulgated.

I think there are problems with the enforcement of the law as it was passed. The almost grim occasion we have had to observe this has been in the case of the Burke Shiley heart valve now finally taken out of circulation, at least the ones that are not implanted, but roughly 200 have broken and about 120 people are dead, mostly Americans. This was a Class III device. It was premarket tested. We believe the FDA sooner than it did should have taken it out of circulation.

There is a problem of adequate enforcement of the law as it is but the law itself does need to be made stronger particularly with respect to making more explicit the criteria for Class III. Anything that is life supporting, as you heard this morning, an incubator is clearly life supporting. It is not as the parents said, just what is inside the patient, but what's outside, the environment, if it is life supporting, just as much as an implantable device needs to be premarket tested.

I would advocate having a much stricter criteria for automatic inclusion in Class III, not allowing the discretion to put it in Class II for which no standards are set and second, the 510(k) has to be redone. The "substantially equivalent" notion has been abused to the point where one wouldn't even recognize some of the devices which incrementally, step by step, have moved away from what they looked like before 1976.

Mr. **Waxman**. We patterned the device laws, at least when it came to devices that offered some kind of exposure to potentially dangerous situations, we patterned the law on the drug part of FDA's responsibility, where they had to approve a device as they had to approve a drug to be safe and effective before it could be sold, yet very little premarket approval seems to get done.

Why did we succeed in the area of drugs but we haven't succeeded in the area of devices?

Mr. **Wolfe**. Well, as you know, I would not say we have fully succeeded in the area of drugs. One of the reasons there are problems with drugs is that two companies, for example, Lilly and Smith Klein, have pled guilty to criminal charges of withholding data, but I think the process is a better one. If a company decides they want to market a new tranquilizer which has only one tiny change in the molecule from one already on the market, one might say it is "substantially equivalent" and yet they are forced to go back to ground zero and do premarket testing for safety and effectiveness of that drug.

In the case of a device, however, if it is used for the same thing and little else, the FDA says, agreeing with the company, it is substantially equivalent and there is no premarket testing. You have heard stories of pacemakers and incubators and other things that were either not premarket tested or other problems happened.

The second example beyond the substantially equivalent one, which distinguishes devices from drugs, is the standard setting category.

Mr. **Waxman**. Would you eliminate the 510(k) procedure completely and require all premarket approvals and all the tests to be done to show it is safe and effective?

Mr. **Wolfe**. I think if one would change the concept of "substantially equivalent" to one that is more like identical or almost identical, I think if you look back at the kinds of devices that have been deemed "substantially equivalent," they are really much more different than they are alike. I don't think there should be no possibility of the FDA ever granting an exemption from premarket testing or standards on the grounds of "substantially equivalent." I think the language has been written or interpreted or both in such a way that it has been abused in a really terrible kind of way.

Mr. **Waxman**. I thank you very much for your testimony and your continued interest in this whole area and we will look forward to working with you.

Mr. **Wolfe**. Your staff knows I am at your service for anything we can do and hope to work together to strengthen these important laws.

Mr. **Waxman**. Thank you very much.

We would like to ask the following witnesses to come to the table, please. From the General Accounting Office, Ms. Eleanor Chelimsky and Mr. Kwai-Cheung Chan. Also Mr. Stephen Ferguson and Mr. William Cook from the Cook Company.

Mr. Ferguson, why don't we start with you? We have all your prepared statements and they will be made a part of the record in full and we would like to ask you, if you would, to try to summarize your oral testimony or keep it as close to 5 minutes as possible.

STATEMENTS OF STEPHEN L. FERGUSON, PRESIDENT, CFC, INC., AND ELEANOR CHELIMSKY, DIRECTOR, PROGRAM EVALUATION AND METHODOLOGY DIVISION, GENERAL ACCOUNTING OFFICE, ACCOMPANIED BY KWAI-CHEUNG CHAN, GROUP DIRECTOR

Mr. **Ferguson**. Thank you, Mr. Chairman. I am Stephen L. Ferguson, President of CFC, Inc., one of the Cook Group Companies, and I have with me, William A. Cook, President and Founder of the Cook Group.

The origin of Cook Group dates to 1963 when Bill Cook and his wife Gayle started the company and began fabrication of diagnostic catheters, wire guides, and needles in the spare room of their apartment. The company is now the largest privately held medical manufacturer of medical devices in the world, producing over 4,000 different products for diagnosis and treatment of disease. There are 34 companies which comprise the Group.

No other manufacturer in the world has the history, expertise, methodology and experience to originate and produce products rapidly for multiple medical disciplines. The company is probably the most innovative medical device manufacturer in the world.

Everyone in this room or someone close to you will require one of the 90 devices that are now under development by the company. Similar to AZT in the treatment of AIDS, technologically superior devices may be your only alternative to treatment. I'm speaking for everyone in this country who is being denied the benefit of treatment under the present system of regulation.

How can this statement be made? As your charts show, in 1985, only 37 premarket approvals were made and in 1986, the number was 72, according to the annual report of the Office of Device Evaluation. In addition, this report also states that only 4 technological breakthrough products were approved in 1986.

These facts are devastating when the entire medical industry is considered and when our company alone, and I repeat, our company alone has 90 products presently under development.

One of the high technology products which treats and cures cancer using heat will take 6 years to reach the market. Our investigation so far demonstrates that this product is safe and ready to use now. Tens of thousands of people are being denied the opportunity to live or have an improved quality of life if this takes 6 years to reach the market.

The bottom line is the new devices are being withheld from physicians and their patients as a result of the regulatory procedures.

In the limited time I have available, I think the following points need to be made.

One, the risk/benefit evaluation of products is lost in a system that may require 100 percent safety. This criteria denies tens of thousands of people the choice, that is, is a 50/50 chance to live better than 100 percent chance to die. New products that have the highest risk in many cases have the greatest benefit.

Two, most physicians, companies and clinicians are not capable of dealing with the system when new products evolve. The result is we lose the benefit of their new product contributions to health care.

Three, the system by slowing or stopping the development of new products has become a regulatory patent which protects current products and denies, I repeat, denies the patient the availability of new treatment. Obviously, many manufacturers can protect their products' sales because their product is approved and a similar or better device created by a competitor cannot undergo the costs and time for approval.

Four, there are thousands of products which have a limited use and would benefit only a few patients that are not being provided to the medical profession because the cost of approval is too high and the red tape is enormous.

We must find a way to handle the low volume, minimum use of beneficial products.

Five, the FDA has been given an impossible task. There is no way they become proficient in all disciplines, procedures and technologies that are needed to participate in the developmental process. During development, products and product changes are necessary and must be made quickly by an informed individual. Product development is a very descriptive term because it connotes change. If a product is to be made better or more practical in use, change must be made efficiently.

Sixth, the regulatory process has moved the doctrine of informed consent from the patient/doctor to Washington, D.C., even with a knowledgeable staff, fulfilling the requirements of the law, it would be difficult because the special interests of Congress may demand 100 percent safety from the FDA.

If the FDA denies categorically the use of a medical device, a physician has fewer or no alternatives that can be offered to the patient. It is the physician's duty to inform the patient of the nature of the proposed treatment, the risk involved, available alternatives and the likely benefits. Such disclosure by the doctor in an informed consent provides the patient with the option so they, the doctor and the patient together can make an intelligent decision.

Neither the FDA as a regulatory agency nor the manufacturer can replace the doctor when he presents the patient with the choice of treatment and the patient and the doctor make an intelligent decision.

The patient having a 50/50 chance to live or have an improved quality of life should have the opportunity to assess the risk with the doctor. For his part, the doctor must be skilled in the use of the product before he can ask for an informed consent.

A poor result because of misuse or inferior product design results in severe punishment to both the patient, the hospital and the manufacturer under our legal system.

Just a few examples of the products that are being withheld from the public by the current system is first of all computer controlled thermal heat probes or hypothermia, which is use of controlled heat sources in the treatment of brain tumors or tumors in any part of the body.

Second, the vena cava filters, which are devices used to prevent clots from entering the lungs through the great veins of the body.

Third, vascular stents. These devices are inserted into the arteries and veins to increase their size or hold them open and they may be used anywhere in the body where blood vessels are closed or are in danger of closing. These devices can reduce the need for or eliminate entirely open heart surgery and peripheral vascular and coronary artery surgery.

Four, the exercise responsive pacemaker. This device can control heart rate according to the amount of exercise. The pacemaker rate is controlled by the temperature variations of the blood. This revolutionary device represents the only true physiological pacemaker.

These are but a few of literally thousands of devices that are awaiting approval for use and which only then can become an alternative treatment. Should the existing process continue for these devices, it will be the year 1999 before they will benefit the general public.

In 1986, Cook had a reported complication rate of .000086 percent out of 8.2 million product uses. Safety and effectiveness is a prime consideration in development and use of any device, but we must not allow thousands to die in pursuit of 100 percent safety. New products must reach the users in a more timely manner.

We must find a way to develop new products which are safe and effective without allowing thousands of people to suffer because the process is too slow.

Thank you, Mr. Chairman. We appreciate the opportunity to appear and we would be happy to answer any questions.

[The prepared statement of Mr. Ferguson follows:]

Statement of Stephen L. Ferguson

I am Stephen L. Ferguson, President of CFC, Inc., one of the Cook Group Companies and I have with me William A. Cook, President and Founder of Cook Group.

The origin of Cook Group, Inc. dates to 1963 when Bill Cook and his wife Gayle started the company and began fabrication of catheters, wire guides, and needles in the bedroom of their apartment in Bloomington, Indiana. The company is now one of the largest medical device manufacturers in the world producing over 4,000 different products for diagnosis and treatment of disease. No other manufacturer in the country has the history, expertise, methodology and experience to originate and produce products rapidly for multiple medical disciplines. The Cook Group Companies are probably the most innovative medical product manufacturers in the world.

Everyone in this room will someday want one of the 90 products we have under development as the best available choice for yourselves or someone close to you just as the AIDS victims wanted AZT. We are speaking for every person in this country who is denied a product as the best available choice under the current system.

In 1985 only 37 PMA's were approved and in 1986 only 72 approvals were made. In addition, the Annual Report of the Office of Device Evaluation points out only four "technological breakthrough" medical devices were approved in 1986. This is a devastatingly low number for the whole healthcare industry when Cook Group Companies alone have 90 products under development. When all manufacturers in the Nation are considered there are thousands of products waiting.

As an example, if it takes 6 years or more to reach the market with the hypothermia probe used to treat cancer tumors, tens of thousands of people will be denied the opportunity to live or have an improved quality of life.

New devices are being withheld from doctors and patients as a result of FDA regulatory procedures.

In the limited time available I think the following points have to be made:

1. The risk-benefit evaluation of products is lost with the system requiring all products to be 100 percent safe and effective denying tens of thousands of people the best available choice. A 50/50 chance to live is better than a 100 percent chance to die. New products which have the highest risk may also have the greatest benefit.
2. Most doctors, companies, and clinicians are not capable of dealing with the system in developing new products, and their contributions to healthcare are lost.
3. The system by slowing development of new products has become a regulatory patent which protects the current products and *denies*, I repeat, denies the patient the availability of new treatment. Obviously many manufacturers support this protection for their products which are currently approved to the market.
4. There are thousands of products which would benefit a few people a great deal which *are not* being produced because of the cost and red tape. A little-noticed result of restrictive regulation is that limited-use devices may never be developed at all. Products which would benefit only a few patients will not be offered because the cost to develop will be too high. We must find a way to handle all of the future low-volume products or new medical concepts having limited use.
5. The FDA has been given an impossible task. There is no way for FDA personnel to be qualified in all disciplines required to participate in development of new products. Product changes are frequent and mandatory during the developmental process. When a design change is necessary it is important that it be made quickly. Product development is a very descriptive term because it connotes change. If a product is to be made better, or more practical to use, change must be made and made efficiently.
6. The process has moved the doctrine of informed consent from the doctor-patient relationship to Washington, DC. Even with a knowledgeable staff, fulfilling the requirements of the law would be difficult because special public interests and Congress demand 100 percent safety from the FDA. This is an impossible situation for the clinician, the FDA staff, its review panels, and the manufacturers.

If the FDA categorically denies approval for a medical device, the physician has fewer or no alternatives that can be presented to the patient. It is the physician's duty to disclose to the patient the nature of the proposed treatment, the risk involved, available alternatives, and the likely benefits. Such disclosure via the informed consent doctrine gives the patient options so that they, the doctor and patient, together can make an intelligent decision. Neither the FDA as a regulatory agency nor the manufacturer can replace the doctor when he presents the patient with alternatives to treatment and then seeks the patient's consent.

The patient having even a 50/50 chance to live or to improve life quality should have the opportunity to assess the risk with the doctor. For his part, the doctor must be skilled in the use of a product before he can ask for informed consent to proceed.

Just a few examples of devices being denied the public by the process are:

Thermal Heat Probes—Hypothermia which is the use of controlled heat sources in the treatment of brain tumors. This involves several probes that can be inserted into the tumor(s) with extreme precision and temperature control. The device is computer controlled and has been shown unequivocally that it is safe to use. Though under investigation for 3 years, it is still not approved. It can be used for tumors in virtually every organ. But until recently was only approved for trial or clinical use in the brain and only then when chemotherapy and radiation treatments had reached their limits for an individual patient and there was no further medical expectations, other than death, without the availability of heat probes.

Vena Cava Filters—These devices are used to prevent clots from entering the lungs through the great veins of the body, and are used on patients with broken hips or thrombophlebitis. A vena cava filter has been developed in Europe and is being sold and used there. The approval process for the European filter is too costly for introduction into this country. It could help patients in this country who have no alternative.

Vascular Stents—These devices are inserted into arteries and veins to increase their size or to hold them open, and may be used anywhere in the body where blood vessels are closed or are in danger of closing. These devices can reduce the need for, or eliminate entirely, open heart and peripheral vascular and coronary artery surgery.

Exercise Responsive Pacemakers—These devices can control heart rate according to the amount of exercise; pacemaker rate is controlled by increased temperature of the blood. This revolutionary device represents the only true physiological pacemaker.

These are but a few of the literally hundreds of devices which are awaiting approval for use and which only then become an alternative treatment. Should the existing regulatory process continue, it will be the year 1999 before many of them will be of any benefit to the general public.

In 1986 Cook, Inc. had a reported complication rate of .000086 percent out of 8.2 million uses. We have no quarrel with regulatory control whose objective is to promote safety provided that people do not die needlessly because of the control and provided products reach the user in a timely manner. The final question we must ask ourselves is, "Should thousands suffer because the system denies them products they need?"

We must find a way to develop new products which are safe and effective without allowing thousands of people to die or suffer because the process is too slow.

Thank you Mr. Chairman and Members of the Committee. Your decision will affect millions of people.

Mr. **Waxman**. Thank you, Mr. Ferguson and Mr. Cook. We appreciate your testimony.

Ms. Chelimsky.

STATEMENT OF ELEANOR CHELIMSKY

Ms. **Chelimsky**. Thank you, Mr. Chairman.

It is a great pleasure to be here this morning. Thank you for inviting us. I am going to be talking about the findings of a study that GAO did recently about reporting problems with medical devices after the Federal Drug Administration clears them for general use by the public.

Let me first introduce the people who are here with me. I have Dr. Kwai-Cheung Chan here, who was our study director, and I also have with me Dr. Gerald Dillingham, who was the project manager for the study, so if there are any details of the study that you want to hear about, we will be able to respond to you.

In the interest of the subcommittee's time, I thought what I would do is not walk you through the statement that you have but simply summarize very succinctly what the findings are and ask that the full statement be made a part of the record if that is possible.

We thought it was important to do this study for two reasons. First, the administrative and state of the art problems that currently exist in pre-testing medical devices signify that, even using the best methods, certain devices are going to be approved when there is still considerable uncertainty about their safety.

This means it is very important for the public's protection to have a communication system operating that can warn FDA swiftly and surely about problems occurring after a device has entered the marketplace. Put another way, if you have got an awfully good reporting system going, you can perhaps take a few more chances of the sort that you are being asked to take early on. If you haven't got a good reporting system, then I think you really have a problem up front.

Second, we knew that the medical device reporting rule would be going into effect, so we wanted to examine the early warning communication system to see whether the only problems lay in manufacturers reporting to the FDA as the rule implicitly assumes, or whether there are other links in the reporting chain that also present problems.

Our study asked four basic questions. First, given a sample of 10 devices, what problems had hospitals, in fact, experienced for those devices? Second, if problems have occurred, do they get reported? If so, to whom and how? Third, how selective has reporting been and what factors influence that selectivity? Fourth, how strong is our early warning system for medical devices overall, and what, if anything, needs to be done to improve or supplement it?

The methodology we used to answer these questions is described in our report and in my statement. Let me just mention here that our study covered a nationally representative sample of community hospitals and is therefore generalizable to the Nation. The sample included 2038 hospitals, and our response rates were 81 percent for the initial survey, 78 percent for the followup.

I have four sets of findings to report related to each of the four questions. First, regarding problems experienced with the 10 medical devices, we were able to identify 1,175 separate problems. Now, these ranged from minor incidents with no adverse effects on patients to an incident involving the death of a patient.

Patient burns accounted for 35 percent of the injuries. That is, they were the chief, the most important problems. Operating rooms of hospitals were the site of 28 percent of the problems. Intensive care units saw 21 percent, and 18 percent occurred on general care floors.

The wear and deterioration of devices was the most frequently reported cause of problems.

Second, with regard to whether problems get reported or not, we found that only 51 percent of the problems identified to us by hospital personnel were ever reported outside the hospitals, and 83 percent of those were transmitted orally. Although hospital respondents identified 46 percent of the problems as having been sent specifically to manufacturers and distributors, when we went to look for them, we could find only 12 percent of these reports or messages in the intended recipient's central files. So if you were going to characterize the reported rate of their communications, you would have had a very low rate compared to what had actually been indicated at the beginning.

Finally, and this is the most important thing, less than 1 percent of the problems in our sample ever made their way to FDA's files. Less than 1 percent.

The third question had to do with selectivity, and here the most disturbing finding from a public safety perspective was that when a problem involved an injury to a patient, a report from the hospital to an outside organization was less likely to be made than if no injury had occurred. The incident I mentioned earlier involving the death of a patient was among those that went unreported.

Also, although hospital personnel had told us that wear and deterioration of devices was the most frequent cause of problems, these types of problems turned out to be the least likely to be reported. On the other hand, the existence of a manufacturer's warranty, a service contract or an exchange agreement spurred reporting. Problems with devices covered by these agreements were reported twice as often as those that were not covered.

So you can see there is a tendency for problems with newer devices to be reported more than those for older devices.

Finally, we conclude that the early warning system for medical devices is not working very well, and we believe that even if the medical device reporting rule should considerably augment the number of problem reports to FDA, other things still need to be done to account for all the links in the communications network. After all, if we don't know a large number of the incidents that are occurring, we are not going to be able to choose which are the most serious ones, and obviously, those are the ones that we have to make some priority system to deal with.

So we think that independent distributors should be included in the mandatory reporting rule. We think that hospital personnel need to be made more aware of how to report medical device problems directly to the FDA. One of the extraordinary things we found was that there didn't seem to be any understanding on the part of hospital personnel that they could report directly to FDA.

We think a voluntary system should be established involving a nationally representative sample of hospitals that would report directly to device manufacturers, and perhaps some new incentives need to be created so that more serious problems and problems involving the wear and deterioration of older devices are more likely to be reported.

That concludes my prepared statement, Mr. Chairman. I would be happy to answer any questions you might have.

[Testimony resumes on p. 379.]

[The prepared statement of Ms. Chelimsky follows:]

STATEMENT OF ELEANOR CHELIMSKY

It is a pleasure to be here this morning to share with the Subcommittee some of the information we have developed regarding the postmarketing surveillance of medical devices. The results I present here come from GAO's recently released study of how the Food and Drug Administration (FDA) monitors the safety of medical devices that have been approved for use by the general public.[1] Our study dealt essentially with the structure and operation of the communications network and other related activities that make up what is known as FDA's postmarketing surveillance system, a system intended to produce early warnings or alerts to problems with medical devices.

Our review had two principal objectives. The first was to describe the communications network and the flow of information for problems associated with medical devices as it existed before the implementation of the medical-devices reporting rule.[2] Our second objective was to determine the degree to which the existing communications network functions as an early warning signal for both FDA and device manufacturers, so that timely action can be taken to protect the public from harm.

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[1] GAO, Medical Devices: Early Warning of Problems Is Hampered by Severe Underreporting, GAO/PEMD-87-1 (Washington, D.C.: December 1986).

[2] Our fieldwork was conducted from March 1985 through January 1986 and requested information about problems that had occurred in calendar year 1984. The medical-device reporting rule that went into effect on December 13, 1984, requires manufacturers to report to FDA when they receive or otherwise become aware of information that reasonably suggests that one of their marketed devices has caused or contributed to serious injury or death or has malfunctioned and is likely to cause or contribute to serious injury if the malfunction recurs.

Because of information developed as the result of several congressional hearings held in 1982-83 and GAO's 1983 report that suggested that the information flow from FDA's postmarketing surveillance of devices was not informing either FDA or the public about the potential danger of some medical devices, we thought it was important to examine exactly how information about medical-device problems originating in hospitals was being communicated outside the hospitals and how device manufacturers and FDA were responding to these problems.[3]

Our focus was thus the communications network rather than individual devices, and we were looking at the likelihood of getting timely information on problems rather than at the problems themselves.

We surveyed hospital personnel working in a nationally representative sample of community hospitals.[4] We asked respondents about their experience of safety with 1 of 10 devices in a sample we selected and about the actions they had taken with regard to specific problems they had had.[5] And if one of the actions they had reported was to notify an organization outside the hospital (device manufacturer, device distributor, FDA, or some other), we then contacted the organizations that had been notified. We repeated this procedure with each organization until we found that the report of the problem had reached FDA or until an organization indicated that it had not received or had not forwarded the message about the problem. Generalizing from the sample, we identified 1,175 separate problems.[6]

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[3] GAO, Federal Regulation of Medical Devices -- Problems Still To Be Overcome, GAO/HRD-83-53 (Washington, D.C.: September 1983).

[4] Community hospitals include all nonfederal, short-term, general and other special hospitals. They represent 65 percent of all hospitals in the United States and 76 percent of all acute-care community facilities. We excluded long-term-care facilities and hospitals with fewer than 50 beds because of the limited number of devices routinely used in these facilities. Eighty-one percent

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(1,651) of the 2,038 that received our initial screening questionnaires returned at least one questionnaire. Seventy-eight percent of the individuals who identified a problem on the screening questionnaire and received our second, more detailed questionnaire returned it.

[5] We used what is known as an "extreme case strategy" to select the sample of 10 devices. Since thousands of devices are in use and our resources were limited, we focused on devices that a panel of experts believed were sufficiently problematic to have led to problems and continuing information transmissions within the postmarketing surveillance system. This strategy allowed us to maximize our chances of obtaining reports of problems and of following their communications through the system. The devices selected were replacement heart valve, intraocular lens, hemodialysis system and accessories, tracheal tube and inflatable tracheal tube cuff, infusion pump and controller, anesthesia gas machine, infant radiant warmer, electrosurgical cutting and coagulation device and accessories, pneumatic tourniquet, and arrhythmia detector and alarm.

[6] The 1,175 problems that are discussed in this testimony represent the number of problems that we would have obtained if we had sent questionnaires to the universe of all hospitals asking for one significant problem from each hospital. The sampling error is 115. This means that with repeated samples of this size, one could expect 95 of 100 times that the total number of problems would range from 1,060 to 1,290.

My remarks today will focus, first, on the nature and extent of the information associated with medical-device problems that flowed from hospitals to device manufacturers and from device manufacturers to FDA and, second, on the impact that this information flow has on FDA's ability to ensure the safety of marketed medical devices.

THE PROBLEMS IDENTIFIED BY HOSPITAL PERSONNEL

In our survey, hospital personnel indicated awareness of medical-device problems with each device in our sample of 10 devices. These problems ranged from relatively minor incidents, with no adverse effects on patients, to an incident associated with the death of a patient. For the 10 devices we studied, actual injuries to patients were associated with 9 percent of the problems identified. The potential for serious injury or death was reported in 37 percent of the cases.

Patients' burns were the most frequent type of injury, at 35 percent, but no other single type of injury (e.g., shock or lacerations) accounted for more than 7 percent of the reported injuries.

The largest proportion of the problems associated with our sample of medical devices, 28 percent, occurred in the operating room of a hospital. This was followed by intensive care units, 21 percent, and 18 percent on the general care floors of the hospitals.

The hospital personnel cited wear and deterioration of the devices as the sole or major cause of the problem in about one third of the cases. Other frequently cited causes were defective components, design flaws, and improper use.

FDA's Communications Network

The four main channels through which FDA can receive information about problems with devices are (1) directly from hospitals; (2) through FDA's problem reporting program, operated by the United States Pharmacopeia Convention (USPC); (3) through third-party monitoring organizations; and (4) through device manufacturers and independent distributors.

We found a severe reduction or "funneling" effect in the nature and amount of information as it moved from the point at which the problems occurred in the hospitals to the point at which messages were transmitted or received by device manufacturers, FDA, and others. Overall, of the 1,175 problems associated with devices that were identified in our survey, only 593, or about 51 percent, were reported to any organization outside the hospitals.

Specifically, in the first channel we found that no information flowed into the network for at least 41 percent of the incidents hospital personnel identified (perhaps more, if the "don't knows" are accounted for). The second channel, from the hospitals directly to FDA or through USPC, was very seldom used. The third channel, through third-party organizations, provided no information to FDA, even though slightly more than 8 percent of the hospital reports were sent into this channel. Finally, only the fourth channel, through the manufacturers and independent distributors, accounted for many reports. Although our hospital respondents indicated that they sent 46 percent of their external reports into this channel, a closer analysis of the data showed that the information flow was not quite so direct. One or more intermediaries, such as sales representatives, often come between a hospital and a manufacturer's headquarters; blockages and breakdowns in the flow of information could and did occur.[7] When we went to the manufacturers, we found that only 12 percent of the incidents were recorded in their central files.

The sparse records of problems with devices in the manufacturers' files may be partially explained by how messages are diffused after they leave the hospitals. For example, 54 percent of the reports in the manufacturers' channel went only to regional offices, and they may not have been forwarded to a main office. In another example, we found that 12 percent of the hospital reports intended for manufacturers really went to independent distributors, and some of these messages may not have been passed along to the manufacturers. While other examples could be given, the point is that there are a number of places in the communications network where a message might stop.

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[7] FDA distinguishes between two categories of medical-device distributor. Manufacturers are referred to as "distributors" and are subject to the medical-device reporting rule. Companies that are not wholly owned are referred to as "independent distributors" and are not subject to the rule. About 80 percent of the surveys returned to us were identified as transmittals to a manufacturer or distributor that was a wholly owned subsidiary of the device manufacturer, and about 12 percent were transmitted to independent distributors.

The net result is that from all four main channels through which FDA receives information, less than 1 percent of the problems in our sample were ultimately recorded in FDA's files.

Selective Reporting of Types of Problems

We found what appears to be a certain amount of selective reporting in the 51 percent of problems that were reported outside the hospitals. For example, when a problem involved an injury to a patient, an outside report was less likely to be made than if no injury to a patient were involved. Among the unreported incidents uncovered in our study was the one that involved the death of a patient.

We also discovered that how the cause of a problem was cited was related to whether or not the problem was reported outside the hospital. For example, we found that problems that were believed to have been caused by wear or deterioration were the least likely to be reported. This suggests that problems associated with older devices may not be reported outside the hospitals. Another factor exerting a powerful influence on reporting was the existence of a manufacturer's warranty, service contract, or exchange agreement. The reporting rate of devices that were covered by these agreements was almost twice that of devices that were not covered.

We also sought to look at the means by which reports of incidents with devices were transmitted, and we found that some 83 percent of the reports from hospitals to outside organizations were transmitted orally. Since no standard reporting procedures, forms, or formats are required, we can only speculate on the quality of the information, and the possible distortion in the oral information, that was passed along. In sum, our study shows that reporting on device-associated problems that the hospitals themselves voluntarily selected as significant was cut in half at the source -- and most of what did emerge was not formally documented.

CONCLUSIONS

FDA can receive early warning of problems with medical devices only if information flows effectively from the hospitals along the various channels of the communications network. Most importantly, FDA learns of less than 1 percent of the medical-device problems in hospitals. About 9 percent of these problems are associated with injuries, and 37 percent are associated with potential serious injury or death. Taking these findings together, we conclude that important problems with medical devices are unknown to FDA because the communications network between the hospitals and FDA does not work very well.

We realize that 100-percent reporting is not necessary to enable the agency to make appropriate postmarketing regulatory decisions and that it is the agency's role to determine the level of reporting that is required in order to establish the nature and scope of problems related to medical devices. However, we believe that the reporting of serious events, such as those described in the medical-device reporting rule, are the most important for the agency to hear about, and we found in our study that those serious events were the least likely to be reported outside the hospitals. Indeed, whether one considers serious or nonserious events, it is clear that if less than 1 percent of the reports of problems are reaching FDA, the early warning system is in need of improvement. Further, these gaps in the flow of information raise important questions about the nature and scope of problems that can be identified by the regulation.

In response to the comments HHS made on our report, we agreed that the medical-device reporting rule may be a necessary first step in improving the severe underreporting of medical-device problems and in increasing the overall effectiveness of FDA's postmarketing surveillance system. However, we believe this rule is not sufficient. We indicated to HHS that it is reasonable to expect the implementation of the medical-device reporting rule to augment the number of reports that are sent to FDA, but since our study did not include a specific evaluation of the rule, we could not empirically assess its effect. We also pointed out that the medical-device reporting rule does not currently require reporting by independent distributors of medical devices, yet our findings show that the distributors are an important link in communications, that they are notified of the occurrence of problems, and that often they do not transmit this information to manufacturers or FDA. This finding supports the need to include the independent distributors in the mandatory reporting scheme.

Solutions to rectify weaknesses in the network should consider the network as a whole rather than trying to repair or strengthen a single link within it. For a first step toward strengthening the whole network, we have recommended to HHS that independent distributors of medical devices be required to report information about problems to manufacturers, just as manufacturers are required to report to FDA under the medical-device reporting rule. Since our study found that more than 50 percent of the hospital personnel did not know they could report problems directly to FDA or to FDA through USPC, we also recommended the establishment of a more effective cooperative relationship with professional health organizations, in order to develop and distribute educational materials for hospital personnel on FDA's need for early warning information and on how to report medical-device problems.

In addition, we recommended that FDA explore the possibility of establishing a voluntary, postmarketing surveillance system involving a representative sample of hospitals that would report directly to device manufacturers. We made this recommendation because of the void we found in the information on problems with medical devices, the potential harm to the public that could ensue, recent initiatives taken by the Joint Commission on Accreditation of Hospitals, and the extremely cooperative attitude hospitals expressed to us while we were conducting this study.

This concludes my prepared statement. I will be happy to answer any questions you or other members of the Subcommittee have.

Mr. **Waxman**. Is Dr. Chan going to testify independently or is he here to answer questions?

Ms. **Chelimsky**. No, he wasn't going to testify.

Mr. **Waxman**. You found that less than 1 percent of the medical device problems in hospitals ever reach the FDA. I understand that your study was conducted before FDA's new mandatory reporting rule called MDR went into effect.

Ms. **Chelimsky**. That is right.

Mr. **Waxman**. Will MDR solve the problems your study identified?

Ms. **Chelimsky**. I don't think so. I think it will certainly up the number of reports, but the real issue, with 1 percent number that we found, is the proportion that get there. When you realize that DEN was already in existence, it's clear they were getting some reports. The real point is that when we went and traced the number that we were told about, we found they didn't get to FDA. So what that tells you is you have got users that need to report and don't, you have a large number of reports going to individual distributors that are not going to manufacturers, and we also found that they were going to regional offices of manufacturers rather than central offices.

There is a kind of ad hoc quality to this system that means that at about 15 different points in that communications network, it could break down. So simply strengthening the node between the manufacturers and FDA is just going to give you that segment of the communications network. The others are not strengthened thereby.

Mr. **Waxman**. What percentage do you think that might be?

Ms. **Chelimsky**. It would be very hard to tell. You can't make any generalization from our study to the overall number of problems. We just took 10 devices, so we only know what we can estimate for those devices. You couldn't really generalize from that to the universe of all problems with all devices.

You have to remember also that we picked devices that were likely to have problems. I think the great majority of devices don't have problems.

Mr. **Waxman**. Now, you told us that there was selective reporting by hospitals. It particularly concerns me that the more serious an incident is with a medical device, the less likely hospitals are to report it, which is what you told us. Do you have an explanation for this? Why wouldn't hospitals be reporting device problems involving injuries or death?

Ms. **Chelimsky**. I think we can't really answer that question. We would have to lend intentions to people who basically were cooperating with us, telling us what they had found, and then, of course, we went and validated what was reported, to see what, in fact, was communicated further on.

What we are showing you is empirical results. Basically, they told us 46 percent of identified problems with devices went to manufacturers and distributors, and we only found 12 percent. What seems to determine more than anything that something gets reported is that there is a warranty on it. That may tell you what criterion is being used.

Mr. **Waxman**. Dr. Chan, do you want to comment on this? I would think there is a fine line sometimes between a problem with a device and a misuse of that device.

Ms. **Chelimsky**. Exactly.

Mr. **Waxman**. So I would think that if there is a fear that they are going to be accused of a misuse of a device or in fact there was a misuse of the device that could lead to a lawsuit, that they don't particularly want that reported. Do you have any comment?

Ms. **Chelimsky**. That could be the reason, but we don't have data on that.

Mr. **Waxman**. You don't have data on it.

Mr. **Chan**. One interesting observation I can make is that even in our method, we found people were giving us over 30 percent of cases where there was potential misuse, and it is so fascinating that they would tell us that.

The second comment I can make is that we also did an independent, separate questionnaire and asked them, not following the data and incidence but rather asking the people who respond to the question what are some of the incentives and disincentives for reporting or not reporting to FDA or the manufacturer, and we observed that they said the seriousness of events would be the greatest incentive for reporting. What we found in the actual data base speaks differently.

So that is the only observation I give you. There is a natural response when we ask them the reasons why, and yet in actuality, it is not the same thing.

Mr. **Waxman**. Even if we can greatly increase the proportion of devices that FDA reviews for safety and effectiveness, we know that most devices are likely to continue to get on the market through the 510(k) process, so it seems critical that we have the post-marketing system for reporting defects to be as effective as possible. Shouldn't all the links in the network, including hospitals and distributors, be reporting?

Ms. **Chelimsky**. I think they should be reported. The real question hinges on whether it should be mandatory or not. I guess my sense is that—based on FDA's experience but also based on the cooperation that we found in doing the study, where we had wonderful cooperation from hospital personnel that we really didn't expect—my sense is that we could try a voluntary system. I certainly think you have to have some system.

I don't think it is possible to leave the users out of the network. We wouldn't be capturing the most important things if we left them out. But I think a voluntary system would probably be much more acceptable. It would probably be easier for FDA to impose, and it seems to me that if it didn't work, we could then move to something more stringent.

But based on their experience in 1980, they were able to try it, and it does seem to me that it is a real possibility and we ought to at least give it a chance to work. Other people have done it. You know, we looked at another group of agencies that had similar hazard problems and how they went about collecting incidence data on them, and one of the systems that we looked at, the NEISS network, used a voluntary system quite successfully with a probability sample. So that in fact, you can really with a minimum of burden on the hospitals really get it. It seems to me it is worth trying. That is the basis for our——

Mr. **Waxman**. Because we have a voluntary system now for reporting and it hasn't worked.

Ms. **Chelimsky**. Well, we have a voluntary system but we don't have a probability sample. It is not a well-structured, carefully running, very much pushed program. It is very different, what NEISS has and what some of the others do.

Mr. **Waxman**. What is NEISS?

Ms. **Chelimsky**. What does NEISS stand for? I can never remember that.

Mr. **Chan**. It is National Accident Sampling System under the National Highway Traffic Safety. NASS.

Ms. **Chelimsky**. No, that's not the one. It's NEISS. There are so many of these acronyms that you have to deal with. It's the National Electronic Injury Surveillance System, not the accident one.

Mr. **Waxman**. Fine. We will look at that and see what we can learn.

Ms. **Chelimsky**. You will find a description of it in our report with the reasons why we recommended a voluntary system. Perhaps it is unnecessary to be so concerned about the burden on the hospitals, but it does seem to me they do have a lot of burdens of reporting, and if one could do it voluntarily, it would probably work. You certainly can't leave the hospitals out. At present it is tantamount to leaving them out.

Mr. **Waxman**. Thank you for that suggestion.

Mr. Ferguson and Mr. Cook, it seems like the devices you listed are all devices for which you are seeking approval but not through a 510(k) process; is that correct?

Mr. **Ferguson**. Yes. We were primarily concerned with the premarket approval, and most NR products are all Class III.

Mr. **Waxman**. Why aren't you going through a 510(k) process? Is it because they are new, innovative devices and not substantially equivalent to anything else that is on the market?

Mr. **Ferguson**. Several of them are new, innovative products so we are working on those, and the second one is if they are, I think, of a nature that even if you said they were substantially equivalent, they needed to go through the premarket process, according to the FDA.

Mr. **Waxman**. I'm sorry. The last part was you don't think they would qualify for a 510(k)?

Mr. **Ferguson**. No.

Mr. **Waxman**. I see.

I wanted to ask you about the regulatory patents area. You were critical of it. You referred to the fact that it can be so time consuming and expensive to get a device approved by FDA that those who have done so often face little or no competition. So once a manufacturer has gone through the PMA process, it would oppose letting similar products on the market through a substantial equivalence test or moving devices into lower risk classes even where that would be appropriate.

It seems rather ironic that products can be declared substantially equivalent to old medical devices but not to new ones because of purely economic concerns. Let me state that the regulatory patent syndrome can hamper meaningful regulatory form. Companies that have them do not like to give them up and seem to feel entitled to them. Do you think they should?

Or to put it another way, do you think that FDA, which is a health and safety regulator, not an economic regulator, should be required to do premarket approvals for low risk devices simply because some manufacturers once had to get premarket approval and now want to make everyone else do it?

Mr. **Ferguson**. Well, we obviously believe that the free market ought to determine, and the point that we are all trying to accomplish is to improve the health care of the Nation. Just because you have a product that you have taken through the process doesn't mean that you ought to be protected from a new, competitive product which is better coming on the market, if that answers your question.

Mr. **Waxman**. Yes. Your opening comments, I think, highlighted the dilemma that we have. Certainly we want the public to get all these devices because so many of them are going to be so valuable saving lives; on the other hand, we want to make sure that these devices are safe and effective.

You put it in terms of 100 percent effectiveness being the requirement. I think that what might look like 100 percent to you may look somewhat different to FDA or to a consumer using the product. We want to have some sense that these products have been scrutinized before they are on the market.

Do you think that they ought to go right onto the market without FDA approval?

Mr. **Ferguson**. No. We see two or three problems with the current system. One is that, just as a comment, safe and effective, we are thinking more in terms of risk-benefit. Obviously, in the case of a patient who has a brain tumor and is going to be dead within a matter of weeks, an alternative treatment, even though it may only have a 50-50 chance, is much better than the 100 percent chance of death. This is a different category.

We also see that even if you do, as has been pointed out by other witnesses, a total premarket approval, that doesn't necessarily mean there are not going to be problems. Also, we see that a lot of problems occur in the scaleup, and that maybe the emphasis is not in what happens before it goes on the market but that area when you go from the model to production. We see that that is really a difficult hurdle to get over in the production process. There you have problems, and we think there ought to be more emphasis in that area rather than back before.

I would say the other thing is that——

Mr. **Waxman**. How would FDA handle something like that?

Mr. **Ferguson**. They have good manufacturing practices now, and a similar type of procedure in terms of you ought to file and go through a process of saying we are going to go from this to scaleup, and therefore here is how we are going to do it and here is how we are going to manufacture. When you go from the model to the mass production, that causes a lot of the problems.

Some of the problems we have heard about today, it wouldn't make any difference if there were a premarket because they have either been quality control or overuse of the device and longevity, which is not going to solve, obviously, reporting.

But our overall feeling is that yes, products ought to go through the process, and we are not saying that, and they ought to be safe and effective and there ought to be some weighing of the risk and the benefit, but it is very difficult for the personnel at FDA to know as much as the manufacturer does in the development of a product. The state of the technology and the nature of it is that products are so complicated that they need to have the expertise out there, and to have them involved in every little decision and every chance and every change during the developmental process really slows it down.

They ought to let us develop the product, go through the procedure, through the premarket approval, file with them, show them what we are going to do, do it, come back to them and say here is what our results are and here is how we are going to scale up. But don't get involved in every decision because I don't think personally they are ever going to be able to eliminate all the problems or be knowledgeable enough to handle them.

Mr. **Waxman**. I don't believe they will eliminate all the problems, but we want them to be knowledgeable enough to, at least for those devices that offer a threat to life, be able to give some sense that this has been reviewed by the experts at the governmental level so they have a sense that it is going to be reasonably safe and effective. No drug or device is 100 percent safe or effective. There is always a risk-benefit concern, given each individual patient's needs at the moment and evaluating whether to go for one process or another or one device or one drug or another. There are no absolute assurances with these things.

I appreciate your suggestions and we will want to look at them very carefully and review them to see how we can make this whole medical device law serve both purposes: to protect the public from unsafe, ineffective devices, but also to get these devices to the people who need them.

Mr. **Ferguson**. We agree. We don't want unsafe devices out there because it affects us and it affects everyone. We do think there needs to be some more emphasis placed on the scaleup provision, the premarket, and we need to get these devices out to the public because they are the ones that are losing if we don't get them to the patient.

Mr. **Waxman**. Thank you very much. We appreciate your testimony.

Our next witness will be Mr. James Benson, Deputy Director of the Center for Devices and Radiological Health at the Food and Drug Administration. I would like to have Mr. Benson come forward.

While Mr. Benson is taking his seat, let me mention the circumstances under which he appears. Although we had invited FDA some time ago, we understand that Mr. Benson is a last-minute player at this hearing and has had no opportunity to prepare a written statement.

As I understand it, Mr. Benson, you are not in a position to respond to questions relating to future budgets or specific legislative proposals.

We certainly appreciate your appearance, and we will keep the record open for any further written statement that you wish to submit.

But before we turn to questions, do you have any comments that you want to make?

STATEMENT OF JAMES S. BENSON, DEPUTY DIRECTOR, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. **Benson**. Let me thank you for the invitation, whether it was last-minute or not. I appreciate the opportunity of being here.

I don't have a formal statement, as you pointed out. However, I am prepared and welcome the opportunity to discuss with you the workload situation in our medical device program. I would also be pleased to share with you the actions we've taken to deal with some of the workload-related problems facing us, as well as the progress we've made in alleviating workload burdens and improving the overall efficiency of the program.

For issues other than those relating to program workload, and including those, in fact, we'd be happy to provide for the record any information that you or the subcommittee feels is necessary and germane to this morning's hearing.

Let me also say that with me at the table here are Mr. Thomas Scarlett, who is Chief Counsel for FDA, and Mr. Robert Eccleston, who is Assistant Director of our Center.

I would rather just go ahead with questions, Mr. Waxman.

Mr. **Waxman**. Well, we heard complaints from several consumers about a number of medical devices earlier this morning, and without asking you anything about the specifics of those cases, I would like you to explain one point.

Assume that we are factually correct in stating that all of these devices either were Class III or Class II devices. Assume further that we're factually correct in stating that none of these devices went through premarket approval or complies with a performance standard. They simply passed through the 510(k) process based on their substantial equivalence to other products already on the market.

Can you explain how this occurs? I'm not sure that everyone who is here understands that process.

Mr. **Benson**. OK. I'd be happy to attempt to.

The agency receives on the order of 5,000 applications or notifications for products coming to market annually, the so-called 510(k)'s. We receive on the order of 100 premarket applications, which relate to post-amendments Class III products. On average, it takes us 1,200 staff hours to review a PMA, but about 20 hours to review a 510(k), and so basically that's why that distinction is so very important.

One thing I would like to point out that I think may be a little bit misleading from some of the statements that I've heard this morning, is that the 510(k) process is not simply a determination of equivalence, and nothing more.

We basically—and frankly, as a result of some of the hearings that we've had in the past—have taken a very hard look at the 510(k) process. Only recently have we been able to get some guidance into the hands of the reviewers and, in turn, into the hands of manufacturers and anyone else that's interested. That guidance basically says that a new product must be at least as safe as and as efficacious as prior products on the market.

If we have any questions about that—and the first thing we look at is whether this indication—that is, the indication for use—is any different from that for a prior product, and does it raise any safety questions?

If it does, then we would automatically turn it down. If the product gets through that gate—that is, the indication gate—and we see changes in the technology that the product utilizes that raise safety questions, it again would be turned down. If we have questions about either of those two things, we ask for data from the manufacturer. Often this is clinical data. So for many 510(k)'s that come through—especially for life-sustaining products, the pacemaker type products—we would definitely require information such as clinical and pretesting data and so on.

But if I may, let me also comment on——

Mr. **Waxman**. Before you move off that issue, let me offer my opinion. It doesn't make sense to have a process in which most devices go onto the market—not by being found safe and effective—but by being found only as safe and effective as some device produced over a decade ago.

Wouldn't it make sense for FDA to have the authority to require that a later product be somewhat safer than an earlier product that was now essentially outdated?

Mr. **Benson**. Well, I think as the technology evolves, that we would always want to be moving in the direction of increased safety. So something like that does make sense to me, yes.

Mr. **Waxman**. And, of course, the 510(k) process, the way you're interpreting it, allows you to look at those other technological advances to establish safety, not just the equivalence to a previous device on the market; is that correct?

Mr. **Benson**. I would say that we have that ability, and certainly if there are safety questions, we could take action.

Mr. **Waxman**. But the bottomline test is still the safety and effectiveness of the original device; isn't that correct?

Mr. **Benson**. That is true, yes.

Mr. **Waxman**. So we have this murky area where you have to look at the original device, whether it's safe and effective, and then this new device, whether it's equivalent to it, even though there could have been a good number of technological innovations which could make it safer. We ought to make sure that we're holding them to the safer standard, not the antiquated standard that once was considered safe because that was the best we could do.

Mr. **Benson**. Yes.

Mr. **Waxman**. You were going to comment on some other area.

Mr. **Benson**. I just wanted to point out, based on the videotape presentation this morning and your comments afterward, I wanted to assure you that we will go back and look at that product specifically to see if it is, in fact, on the market illegally, as I think you suggested if I heard you right. We'll certainly check that out.

Mr. **Waxman**. We heard earlier about an incubator that apparently was on the market prior to 1976 and was still being used in 1981 when tragedy struck.

Without commenting on that particular case, if you look at the charts—if you look at Chart No. 4, which is the premarket approval backlog, and 5, which is the performance standard backlog—until the FDA reviews pre-1976 Class III devices for safety and effectiveness or writes performance standards for the old Class II devices, new products will continue to get on the market simply by being substantially equivalent to those old ones under the current law, and this will continue year after year, even long after all those old devices are no longer being sold; in fact, until FDA regulates the old devices; isn't that correct?

Do you believe this situation should continue indefinitely? Fifty years from now, should we be comparing devices to pre-1976 devices?

Mr. **Benson**. No, sir, I don't. I think that the premarket Class III products are ones that cause concern. As the chart shows—and, by the way, I think N equals 1 on the righthand column but that's not a significant impact, I would agree—we are looking at that group of products. We have identified 12 products for which we're considering calling for premarket approvals and basically we'd like to get on with that.

We have to do it in a very metered, very measured way, because I think we estimate, if all the pre-Amendments products were called for, that we'd get something on the order of 1,000 PMA's. We don't know exactly, but something on that order. The workload for this I think is around 150 staff years. It may even be more than that; I don't have those figures in front of me.

I think at the same time that, perhaps through post-market surveillance activities, we need also to pay very close attention to those products to see if there are problems.

I think the saving point there is that the products have been out there awhile. We do have postmarket data on them and, if necessary, could take action based on that information. It's certainly not as thorough as premarket approval, but not lacking either.

Mr. **Waxman**. Other than the fact that roughly 50 to 100 devices a year have to go through premarket approval, aren't things pretty much the same for most manufacturers today as they were before the 1976 law was passed?

Before that law was passed, FDA could seize dangerous goods in the marketplace. The only thing it lacked was premarket approval, yet the agency only uses premarket approval for a few devices. So little really has changed.

Mr. **Benson**. I think they are vastly different. I think on the grand scale, just the awareness of the importance of quality control, quality assurance, that has resulted from the Device Amendments makes a difference.

There are specific programs like that for Good Manufacturing Practices, which I'm surprised and delighted to report that the industry in general supports. In fact—I've talked to some of the regulatory affairs people and some of the people in the plants, and they genuinely feel that it has helped them improve their quality. I think we're going to see more growth in that area as we begin to look at things like design validation, something that's not specifically covered in the regulation, but something that many manufacturers are concerned with.

Certainly a program that you were instrumental in getting us rolling on was the mandatory reporting program, which also causes a great difference in the way that industry looks at their products. I think that's borne out if you look at your recall chart over there.

So I think there's a great deal of difference. I think some of the educational programs that we're beginning to get into place also make a difference. And there are many other areas that we could go into in more depth.

Mr. **Waxman**. I realize you're not in a position to discuss specific legislative proposals, but let me just ask you generally: Without some fundamental change in the law, aren't we likely to be here 10 years from now holding essentially the same hearing with essentially the same charts?

Mr. **Benson**. Let me digress a minute on that question. When I became associated with the medical device program—starting back in 1982—I think it was fairly clear to me coming in fresh that there were severe problems. Certainly those problems were illustrated in the various oversight hearings that have been held. And I think that the conclusion that many of us came to very rapidly was that we needed either to change the law or we needed to change the practices that were presently in place.

And I think that we have made a lot of progress toward changing those practices, and so I feel very good about that personally, and I think organizationally we're proud of the changes that have been made.

On the other hand, I think that if you look at the overall staffing of the Federal Government, FDA included, going back over the past 5 years or so, FDA's staffing has diminished—I don't know what it is; something on the order of 5 percent. Our center's staffing over roughly the same time period has also diminished by about the same percentage.

We feel very fortunate that in the last year or so the Commissioner has been able to increase our staff by about 40 staff years, and we look forward to some modest increases in the future. But I think that because of all the programs that we see coming down, we've had a workload increase of something like 115 percent in some areas in that same period of time with applications. We've had new programs that have come along—MDR, the pacemaker registry. The fact that we're trying to pay more attention to our science base, the fact that we're trying to get educational programs off the ground, and so on—means that in a lot of these areas you're not going to see strong improvement, and mandatory performance standards is a good example.

I would think that, if I have anything to do with it, you'll see a few mandatory standards in place at the end of that 10-year period, but you're not going to see a significant dent in the backlog that the chart illustrates.

Mr. **Waxman**. OK. Thank you very much for your testimony to us. We look forward to working with you and FDA in looking at legislation.

Mr. **Benson**. Thank you, and thank you for having us.

Mr. **Waxman**. Let me ask if Mr. James Young has arrived? If you could come forward. Good.

Welcome to the subcommittee meeting. I understand you've just arrived from Florida this morning.

What we'd like to ask you to do is to take 5 minutes and tell us about your medical device experience to us, so it will be helpful as we evaluate the medical device legislation.

STATEMENT OF JAMES YOUNG, SARASOTA, FL.

Mr. **Young**. OK. Good morning.

Mr. **Waxman**. On the base of that mike, there's a button, if you would push it forward.

Mr. **Young**. Good morning. As you know, my name is James Young, and I'm from Florida by way of Boston, MA where I spent all my working years. I retired in 1971 and went to Florida, but found that my pension wasn't enough, so I was semi-retired once I got to Florida. I took a part-time job there.

In 1971, I had a partial knee replacement on my right knee, and this, we knew at the time, was only for a limited duration. I was very fortunate that it lasted 8 years.

In 1984, both knees gave out, and I had to have both knees with total replacements. Quite painful, as I found out. In order to rehabilitate, they put you on a machine which automatically brings your leg up and down, up and down, night and day while you're in the hospital. And I finally got to the point where I had to ask them to take me off the machines, the pain was too great.

I came out of those two operations—I was in there for about 3 weeks, I think. They did one, and 7 days later they did the other one. And it took about, oh, 5 to 6 months before I was able to get back on my job in 1984.

In 1985, I think it was August of 1985, the left knee failed. The prosthesis that they put in there failed. And while I was in the hospital, my doctor came in, and he told me that Dow Chemical told me not to worry about the expense; they were going to take care of it.

When I got back on my feet somewhat after I left the hospital, I had a meeting with a representative from Dow in my doctor's office. And trying to be a good Joe, I told them that if they would take care of my missing wages and the difference between what my insurance company would pay for the operations and what the total bill was, I would be happy. I think it cost them something like $1700, something like that, for an operation that probably would cost around $10,000, and a good portion of the $1,700 was my lost wages.

Now it went along OK, and then I was out there for about 4 months, and I went back to part-time. I could not do the hours that I had before. I was on limited hours at that time. And then in July 1986, the right knee failed.

That's when I got mad, and I got my attorney to see if he could find out something for me, and he said that he had learned from your subcommittee staff that there was no pretesting of these parts that were put in my body. And this really disturbed me, because I'd been through a lot of pain and a lot of rehabilitation.

And I recovered from that one somewhat. That was in July 1986, and I was about ready to get back to work when in August the left knee had to have what they call a lateral release, which had been operated on in 1985. And I just felt like they ought to put zippers in my knees. They kept going back and forth all the time.

The doctor felt that the lateral release was needed because of the two operations on that knee, and he said perhaps the stress of trying to favor the right knee also had something to do with having to go back in on the left knee.

I just can't understand the FDA not testing this product before it goes into the human body. It makes me feel that the human body—well, we're just nothing but a bunch of guinea pigs, and so let's try it out on this guy, see if it works. They never did tell me when they came to the doctor's office to settle on the first one in 1985, they never did tell me that there was a good possibility that the left one was going to fail.

And so I just can't understand why the FDA does not have pretesting before these things are put on the market.

Mr. WAXMAN. Well, we checked the regulatory status of the Lucy Patella implants, which is what you had, with the FDA. As with other devices we heard about this morning, these devices fall into Class III, the group that FDA has designated as requiring premarket approval.

Again, as with these other devices we've heard about, these products have never gone through premarket approval. Instead, they got onto the market by claiming to be substantially equivalent to devices already on the market.

That's what we're looking into this morning, whether that loophole which allows them to establish that they are substantially equivalent to some other device, should be continued as a bootstrap in the way it has been for devices to go on the market, be implanted in people, without a premarket scrutiny, which you would think these kinds of devices deserve.

Mr. YOUNG. Well, I feel that I've had three more operations than I should have had. And as you well know, any time anybody goes under anesthesia, their life is in danger, and I feel that my life has been endangered three more times than it should have been.

Mr. WAXMAN. Well, I want to thank you very much for coming all this way to share this with us. I think it's helpful for us to understand this whole medical device issue in the human perspective of what happens to people, in not just the academic sense of, "Well, we'll make some kind of substantial equivalence, and isn't that good enough," because obviously in your case and in other cases, it doesn't appear that it was good enough. And you expected, as others expect, that the Food and Drug Administration is protecting you from drugs and devices that may not be safe and effective.

Thank you very much for coming here today.

Mr. YOUNG. Thank you.

Mr. Waxman. That concludes the hearing this morning. We stand adjourned.

[Whereupon, at 12 noon, the hearing was adjourned.]

[The following statement was submitted for the record:]

STATEMENT OF GERRY SIKORSKI

June 16, 1987

Mr. Chairman:

Thank you for holding open the record of the May 4 hearing of the House Energy and Commerce Committee's Subcommittee on Health and the Environment. As you know, my schedule kept me from being in attendance. This hearing, which focused on medical device product problems and the FDA's product approval process, raised significant policy issues, and I look forward to working with you in this very important area.

After this hearing took place, it came to my attention that one of the witnesses -- Mrs. Pam Taylor, the mother of a young girl who had received a pacemaker implant -- made certain statements regarding the performance of a pacemaker lead that do not appear to be supported by the facts. The lead in question (Model 4951) was manufactured by Medtronic, an industry leader, which is headquartered in Minnesota. Mrs. Taylor told the Subcommittee that this Medtronic lead, which had been implanted in her daughter, Jessica, failed, and that it was defective. I would like the Subcommittee to know that our information is that the Medtronic Model 4951 lead has an excellent performance record, and that the problems experienced by Mrs. Taylor's daughter appear to be unrelated to the performance of this pacemaker lead.

I would like to take this opportunity to submit a brief background paper, which outlines the facts of the situation. Appended to this paper are three items bearing on the claims made by Mrs. Taylor at this hearing:

> A copy of the deposition of J. Terrance Davis, M.D., the implanting physician, to the effect that the underlying cause of the reoperative procedure was due to the intrinsic problem of the patient's heart, not to any problem with the lead or the pacemaker.
>
> A statement by Robert G. Hauser, M.D., consultant to Pacesetter Systems, Inc., the manufacturer of Jessica's pacemaker, that "there is no reason to believe that the Pacesetter pulse generator was at fault, that the leads were at fault, or that the physicians were at fault."
>
> A list of several articles by American and British physicians with respect to the same phenomenon Jessica experienced relating to "Exit Block in Children with Pacemakers." Nearly 50% of pediatric patients experience the same problem of fibrotic growth in the heart, rendering the lead and pacemaker ineffectual, even though they are functioning perfectly.

Thank you again, Mr. Chairman, for allowing me to correct the record.

BACKGROUND

The Model 4951 Unipolar Lead

Performance of the Model 4951 lead has been excellent.

- Returned product analyses show failures of less than two-tenths of one percent (0.2%).
- More than 10,000 of these leads have been implanted.

The Model 4951 lead was market released in May 1982 through the FDA's 510(k) product approval process.

The Patient/Treatment

Jessica Taylor, a nineteen-month old child, received a bipolar Pacesetter pulse generator (Pacemaker Model 226-6, Serial No. 15462), along with two (2) Medtronic leads (Model 4951-53, Serial Nos. TF0010285R and TF0010272R) on October 25, 1982.

On October 10, 1983, the bipolar Pacesetter pulse generator that had been implanted in Jessica Taylor was replaced with a unipolar Pacesetter pulse generator (Model 261, Serial No. 1001). It was attached to one of the previously-implanted Medtronic 4951 leads which was still functioning. The other Medtronic lead was capped to avoid any unintended electrical contact, and was left implanted. The record shows that there were no intraoperational complications, and that the patient tolerated the procedure well.

Testimony/Response

Jessica Taylor's lead did not fail, as Jessica's mother testified at the May 4 hearing of the House Energy and Commerce Committee's Subcommittee on Health and the Environment.

The child's need for a re-implant was not the result of any malfunction of either the Pacesetter pacemaker or the Medtronic lead.

- A physiological reaction to a pacemaker lead frequently occurs in pediatric patients. Because tissue response is greater in growing children than in adults, the area where the lead electrode has contact with the heart is subject to a build-up of fibrotic tissue. At some point, exit block may take place. This means that the amount of energy needed to pace the heart exceeds the output of the pacemaker, so that the heart cannot respond, even though the pacing system functions perfectly.

- As many as 50 percent of pediatric patients experience complications of this nature. By contrast, relatively few adults develop this fibrotic growth.
- The treating physician, Dr. J. Terrance Davis, testified under oath that Jessica was experiencing the problem described above. This problem is the result of common physiological phenomena inherent in the heart itself, and is not the result of any defect in the lead. (Attached is a transcript of Dr. Davis' deposition.)
- Dr. Robert Hauser, an eminent pacing physician who has reviewed the available records on behalf of Pacesetter, has concurred with Dr. Davis' opinion. He stated that Jessica had experienced a well-known complication of cardiac pacing, and that her problems had not occurred as a result of a defective product or improper care. (Attached is Dr. Hauser's statement.)
- The best spokesperson on epicardial leads implanted in pediatric patients is Dr. Paul C. Gillette of Charleston, South Carolina. Dr. Gillette, the immediate past president of the North American Society of Pacing ano Electrophysiology (NASPE), presented several papers on this subject at the annual NASPE meeting earlier this year. (Attached is a listing of relevant articles by Dr. Gillette and other experts on this matter.)

Jessica's mother testified at the May 4 hearing that the Model 4951 lead that had been implanted in her child shared the same characteristics as another Medtronic lead - the Model 6972 lead - which was the subject of a recall in 1984.

- She was mistaken. The only shared technology is the polyurethane insulation of these leads.
- The Model 4951 lead is unipolar; the Model 6972 is bipolar. The Model 4951 lead is epicardial; the Model 6972 lead is transvenous. Further, the fixation characteristics of the two leads are different: the Model 4951 lead is a "hooked" lead; the Model 6972 lead is a "tined" lead.
- The 4951 lead was approved through the FDA's 510(k) product approval process as a lead "substantially equivalent" to two prior Medtronic leads, the Model 6972 lead and the Model 6971 lead. This approval process does not equate the lead implanted in Jessica with the product problem associated with the Model 6972 lead. It should be noted that the Model 6971 lead, in contrast to the Model 6972 lead, has a record of excellent performance.

Conclusion

The Model 4951 lead that was implanted in Jessica has an excellent performance record. It has proven itself to be a safe and effective lead based on a history of more than 10,000 implants.

Medical experts, including Jessica's own implanting physician, see her situation as a physiological complication -- not an instance of a product defect.

There is no reason to conclude that the FDA's 510(k) product approval process led to the inappropriate or unwarranted distribution of the Model 4951 lead.

COPY

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF OHIO

WESTERN DIVISION

JESSICA S. TAYLOR, et al., :
Plaintiffs, :
vs. : Case No. C85-7235
Hon. Richard B. McQuade, Jr.
PACESETTER SYSTEMS, INC., :
et al.,
:
Defendants. :

- - -

Deposition of J. TERRANCE DAVIS, M.D., a Witness herein, called by the Plaintiffs as if upon Direct Examination under the Federal Rules of Civil Procedure, taken before me, Diane L. Perusek, Registered Professional Reporter and Notary Public in and for the State of Ohio, pursuant to agreement and stipulations of Counsel as hereinafter set forth, at the Medical College of Ohio at Toledo, 3000 Arlington Avenue, Toledo, Ohio, on Wednesday, March 11, 1987, at 2:10 p.m.

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Q They're not in your view a symptom of a problem?

A Not necessarily.

MS. LALAK: All right. I have no further questions. Thank you, Doctor.

- - -

CROSS EXAMINATION

BY MR. JONES:

Q Doctor, of course, I have a few questions and hopefully very few. Number one, you have reviewed and signed the deposition that was taken, I believe, on January 21st, 1986; have you not?

A Yes.

Q Or '87, excuse me.

A Yes.

Q Did you find any errors in your testimony as recorded in that deposition when you reviewed it?

A I didn't.

Q Do you reaffirm everything you said in that deposition?

A Yes.

Q One of the things you said in that deposition, Doctor, was that in your medical opinion to a reasonable degree of medical certainty because of the failure to sense, in Jessica's case, not some other case, but in her case, was something that you referred to as a lead tissue interface problem; is that correct?

A Yes.

Q The reason I'm asking this again is that you have testified here today in response to questions by Mr. Jacobs to, number one, statements you made to the mother about possible causes of the problem being anything including the generator, the leads, or Jessica's heart itself. You did say those things to the mother, correct?

A That's correct, yes.

Q Let me ask you a couple more questions about that. It is your opinion, Doctor, is it not, again, that despite the many possible causes of the failure to sense that, in your opinion, because of the resistance measurements that were taken and the results of those measurements, that it's your opinion that in this case the cause of the sensing problem was in Jessica's heart itself?

A That's correct.

Q You were asked and I believe Mr. Jacobs has asked you at some point today about -- or perhaps your responses were that you were guessing or there were - that something was a guess at the causes of her problem in this case, and I want to clarify that statement.

As I understood what you said, Doctor, and correct me if I'm wrong, you've testified here today that you would be guessing as to the exact nature of the tissue problem within Jessica's heart; is that what you were saying?

A Yes.

Q Correct?

A That's correct.

Q You are not meaning to imply to Mr. Jacobs today that you were guessing that the cause was within the heart?

A Once we did the lead measurements, sure, to a reasonable certainty as far as I was able to determine the problem was within the heart because a crack in the insulation would have a very low resistance, which we did not find.

Q Sure, we went through that, of course, in the first deposition. A crack would result in below normal range resistance and a break in the wire would result in higher or infinite resistance, so I'm just trying to clarify the word guessing, and all you were saying is that it would be a guess to describe the specific tissue problem within the heart itself?

A That's right.

Q But it's not a guess to say that the problem was some kind of problem with the heart tissue itself?

A That's correct.

Q I believe I asked you in the first deposition and I'll ask you again because you said it again today. You used the term, bad lead and good lead as you did in your operative notes that we've looked at. Would you explain to us once again what you mean when you use those terms, good and bad lead?

A That is an operational definition to determine a lead that is stimulating the heart and a lead that is not stimulating the heart.

Q It did not mean at the time you wrote it and it does not mean today that one lead was defective and one lead was not?

A That's correct.

MR. JONES: Thank you. That's all I have.

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REDIRECT EXAMINATION

BY MR. JACOBS:

Q I'm reminded of the problem of the pacemaker that's sitting in the vault, and I understand that mother

RUSH-PRESBYTERIAN-ST. LUKE'S MEDICAL CENTER

ROBERT G. HAUSER, M.D.
Director, Pacemaker Surveillance Program

July 17, 1986

Larry Selznick
Manager, Technical Services
Pacesetter Systems, Inc.
12884 Bradley Avenue
Sylmar, California 91342

Re: Jessica Taylor

Dear Mr. Selznick:

I have reviewed the enclosed case of Jessica Taylor who received a Pacesetter pacemaker and epimyocardial leads in October of 1982 for second and third degree AV block. Subsequently, she was readmitted to the hospital for a pericardial effusion which required a pericardiocentesis. Apparently she recovered nicely and all reports indicate that the pacemaker was functioning normally in May of 1983. Then, in the fall of 1983, she experienced several syncopal episodes and was readmitted to the hospital. On October 10, 1983, she underwent a pacemaker procedure. A review of the records of that admission indicate that the pacemaker was not sensing the patient's spontaneous QRS complexes. Attempts to program the pacemaker to a higher sensitivity did not seem to affect the problem. Likewise, increasing the duration of the refractory period did not improve the situation. In the operating room, on October 10, 1983, the amplitude of the bipolar R-wave was found to be 0.2 millivolts, clearly too low for sensing to occur. Therefore, the pulse generator was replaced with a unipolar pulse generator and connected to one of the previously implanted leads. This resulted in a low threshold and adequate R-wave for sensing.

It is quite clear that the problem in this case is a lead-tissue interface anomaly which is not related to either the pulse generator or directly to the lead-electrodes. In addition, it should be noted that, in my opinion, the physicians who cared for this patient exercised good judgement and technique and in no way can I criticize their management of this case.

In summary, in my opinion, there is no reason to believe that the Pacesetter pulse generator was at fault, that the leads were at fault, or

EXHIBIT 2 TO HAUSER AFFIDAVIT

1753 West Congress Parkway Chicago, Illinois 60612

that the physicians were at fault. This is a well-known complication of permanent cardiac pacing, especially when one considers the difficult circumstances surrounding this patient's clinical problem.

Sincerely,

Robert G. Hauser, M.D.

References

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2. Gillette, Paul C.: Cardiac Pacing in Children. In: Riegel, Barbara. et al. DREIFUS' PACEMAKER THERAPY: AN INTERPROFESSIONAL APPROACH. Philadelphia, PA: F. A. Davis, 1986, pp. 201-218.

3. D. G. Wampler, C. Shannon, R.N., Gina V. Burns, R.N., Paul C. Gillette, M.D.: Cardiac Pacing in Children and Young Adults. American Journal of Diseases of Children, 137:1098-1100, Nov. 1983.

4. D. E. Ward, M. Signy, P. Oldershaw, S. Jones, and E. A. Shinebourne: Cardiac Pacing in Children. Archives of Disease in Childhood (London), 57(7):514-520, July 1982.